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# OBSTRUCTION OF THE ŒSOPHAGUS IN CHILDHOOD

BY

WILFRID SHELDON, M.D., M.R.C.P.,

and

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The condition broadly defined by the title of this paper was brought to our notice by the clinical observation of six children at the Hospital for Sick Children, Great Ormond Street, all of whom presented the symptoms of wasting, constipation, and regurgitation of undigested food from the œsophagus. Although the term 'cardiospasm' was applied to these children for the purposes of the hospital records, the underlying morbid condition which existed at the lower end of the œsophagus remained in most cases obscure. In the hope of reaching a clearer understanding of the pathological basis of these cases, the hospital records were searched, and six additional cases of similar nature were found. Of the total of twelve children with œsophageal obstruction, five have died. With one exception these have come to post-mortem examination, and the pathologist's reports have been available. In addition, radiological evidence has been forthcoming in all but two cases.

To be complete, this article should include that form of obstruction met during the first two weeks of life due to complete atresia of the œsophagus. Instances of this condition have been frequently recorded, and in 1917 Cautley[1] published a full review of the subject. The symptoms are well defined, and the condition is incompatible with life, so that further allusion to this group will not be made. Acquired stenosis such as follows upon the ingestion of caustics is also excluded from consideration.

The study of the cases at our disposal was simplified by grouping them according to the level in the œsophagus at which the obstruction occurred, and we shall consider them in this manner. The first and largest group consists of 10 children who had obstruction at the level of the seventh thoracic vertebra, halfway between the level of the bifurcation of the trachea and the diaphragm. It is to these cases that we wish to draw particular attention, because they form a clearly defined clinical entity, which is, however, apt to be confused with the condition called 'cardiospasm' or 'achalasia of the cardia.' The result is that they are often submitted to treatment which, although successful in cardiospasm, is injurious to them.

In the two remaining cases, the obstruction was at the level of the diaphragm,

GROUP 1. (CASES 1—10). OBSTRUCTION AT LEVEL OF 7TH DORSAL VERTEBRA.

Case 1. Previously recorded by Dr. Hutchison.[2] C. F., a male child, was admitted to hospital at the age of 3 years with a history of vomiting since six weeks old. For a week in each month the vomiting was particularly severe, occurring after each meal. Constipation was a constant symptom, varying with the vomiting.

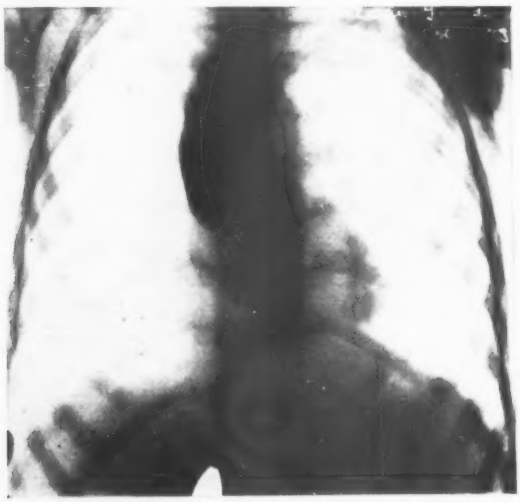

FIG. 1.

FIG. 2.

On examination the child was very undersized (weight 15 lb.). X-ray examination (Fig. 1) showed a bismuth meal retained in the œsophagus at the level of the 7th thoracic vertebra, well above the dome of the diaphragm. The child was given a fluid diet, but continued to vomit every day, and a month later developed a fatal broncho-pneumonia. Bougies were not passed in this case.

At the post-mortem examination, a hard fibrous constriction of the œsophagus was found at a level of 1½ inches below the bifurcation of the trachea, the portion of the œsophagus above the constriction being dilated. Microscopical section through the constriction was not made. The case was regarded at the time as an example of congenital stricture of the œsophagus.

Case 2. R. B., male, was admitted to hospital for the first time at the age of 19 months. Vomiting, which dated from birth, had been worse since weaning on to solid food at 12 months of age. Constipation had accompanied the vomiting.

On examination the child was thin, and weighed 15 lb. There were no abnormal physical signs. Examination by X-ray (Fig. 2) showed a bismuth meal held up in the œsophagus at

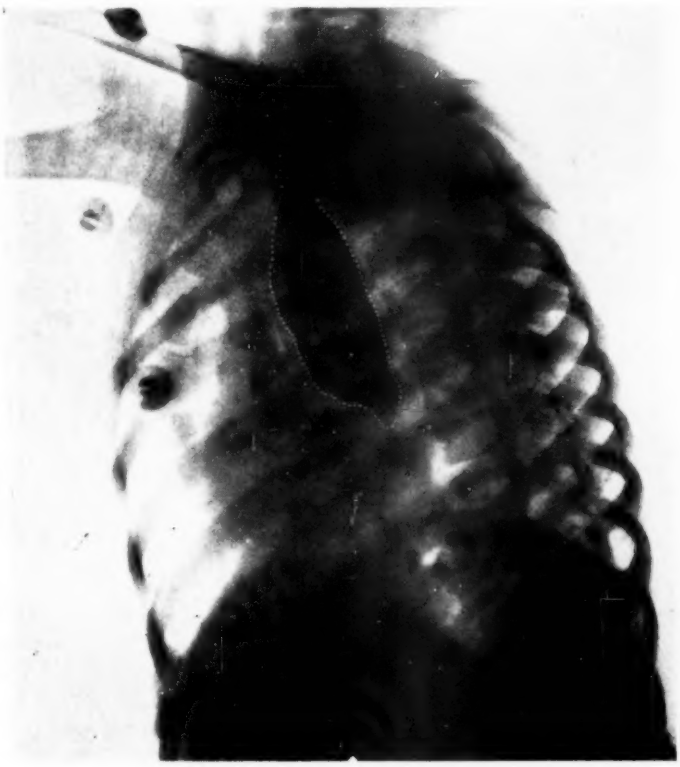

Fig. 3.

the level of the 7th thoracic vertebra, a full inch above the diaphragm. A strictly fluid diet was ordered, and the vomiting was gradually overcome. During the next 5 months the weight increased to 20 lb.

A year later the boy was re-admitted because of a return of persistent vomiting during the previous 3 weeks. An X-ray photograph demonstrated that although the œsophagus was less dilated, the level of obstruction had not altered. A fluid diet was again established, whereupon the patient improved.

The boy was seen again at 6 years of age, when it was learned that attacks of vomiting had recurred at gradually lengthening intervals. There had been no vomiting for the last 10 months. The boy looked well, his weight was 40 lb., and an X-ray screening showed no delay in the passage of an opaque meal into the stomach.

It would appear that in this child the œsophageal obstruction underwent a slow cure. The passage of bougies was never attempted, the only line of treatment being prolonged persistence with a fluid diet.

Case 3. K. A., male, aged 3 years, was admitted to hospital with a history of vomiting immediately after meals since he was 10 days old. Vomiting had become worse after weaning at 3 months of age. Growth had been accompanied by great weakness, so that he was unable to sit up until 12 months, and did not walk until 3 years of age. Constipation had been a constant feature.

On admission he weighed 17 lb. The muscular weakness was so pronounced that the diagnosis of amyotonia congenita was suggested, and the œsophageal condition was at first overlooked. The muscles were very small, especially the buttocks, which resembled the condition described by Miller[3] as occurring in cœliac disease. For several weeks the child vomited all solid food. An X-ray photograph (Fig. 3) taken during this period showed the bismuth meal held up in the œsophagus at the level of the 7th thoracic vertebra, at least an inch above the diaphragm. A fluid diet was established, and after 3 weeks the vomiting gradually ceased. Seen 8 months later, the child had become quite active and was improving steadily. Vomiting occurred occasionally. X-ray screening showed no delay in the passage of food through the œsophagus.

FIG. 4.

This case resembles the preceding one in that bougies were not passed down the œsophagus. A steady improvement was brought about by insistence on a fluid diet.

Case 4. A. H., male, aged 2 years, was admitted to hospital on account of persistent vomiting since birth. Vomiting occurred immediately after meals, but there were occasional periods of freedom from vomiting, on one occasion for as long as 3 weeks. The child had lived on fluids, being unable to keep down solid food. Constipation had been a symptom since birth.

On admission the child was wasted, weighing only 14 lb. X-ray examination (Fig. 4) showed a bismuth meal obstructed in the œsophagus at the level of the 7th dorsal vertebra. A strictly fluid diet was instituted, and at first the child lost weight, and became gravely ill. Eventually the vomiting ceased, and the patient left hospital after 12 months observation, by which time the weight had increased by 2 lb. On discharge instructions were given for the fluid diet to be continued. Unfortunately it has not been possible to trace the further history of this child. Bougies were never passed on this case.

Case 5. V. D., female, was first admitted to hospital when 8 years old. Since the age of 11 months the child had never been able to take solid food, as the attempt to do so always resulted in vomiting.

On admission the girl weighed 44 lb. The only abnormal physical signs consisted of systolic and diastolic murmurs at the apex, denoting an old rheumatic lesion of the heart. X-ray examination (Fig. 5) showed an obstruction in the œsophagus at the level of the 8th thoracic vertebra, well above the diaphragm. Œsophageal bougies were passed without difficulty into the stomach, and this line of treatment, combined with a thickened fluid diet, produced considerable improvement. After 6 weeks the child was able to keep down solid food, and had gained 3 lb. in weight.

Seen again at 11 years of age, the girl weighed 55 lb. After her previous discharge from hospital, the original symptoms had quickly returned, and she had had to subsist on thick fluids such as custard and cornflour. A second X-ray examination showed that the condition of the œsophagus had not improved during the 3 years since the first examination. Treatment by the daily passage of mercury-filled bougies was carried out, and improvement was soon manifest. After 8 weeks the weight had risen by 4 lb., and the girl could swallow and retain solid food.

FIG. 5.

It is interesting to note the improvement that followed upon the use of bougies. Relapse soon followed the cessation of the first course of such treatment. It is as yet too soon to say whether the second course will be followed by more lasting improvement.

Case 6. B. B., male, was admitted to hospital when 5 years old, on account of vomiting after meals since birth. On three occasions he had undergone treatment in a local hospital, and on each occasion had improved on a fluid diet.

On admission the boy weighed 30 lb. There were no abnormal physical signs, and the Wassermann reaction was negative. X-ray examination (Fig. 6) showed a bismuth meal held up in the œsophagus opposite the level of the 7th thoracic vertebra. For 2 months the boy was given a fluid diet, and slowly improved. He then developed measles, and rapidly lost weight. Treatment by the passage daily of a heavy mercury-filled bougie was then instituted. At first a resistance to the passage of the tube was encountered about 9 in. from the teeth, but after a

short delay the tube passed on into the stomach. After 14 days of this regime, the boy was able to pass the tube himself, and he was discharged home with instructions to continue the treatment. He succeeded in doing this for two months, and then abandoned the method.

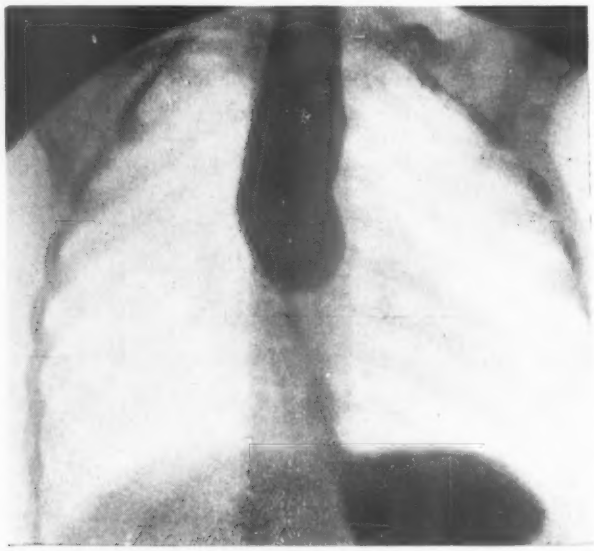

FIG. 6.

FIG. 7.

A month later intractable vomiting returned, and he was readmitted to hospital. Recourse was had to feeding with thickened fluids, and slight improvement was made, although vomiting continued every day. During this time the boy survived an attack of paratyphoid fever, and it is noteworthy that from the first rise of temperature until its fall 3 weeks later he was entirely

free from vomiting. With the subsidence of the fever, vomiting recurred daily. It was now found impossible to pass an ordinary bougie, but under anæsthesia a very fine bougie was passed beyond the stricture. The bougie was left in the œsophagus for 6 weeks, when it was changed for one slightly larger. Vomiting continued intermittently, and 2 months later the child developed a chronic laryngit is which necessitated removal of the tube. It was now possible to pass a heavy mercury-filled bougie (No. 24) without an anæsthetic, and this was done every day. At the time of writing the boy is 7 years old, and weighs 36 lb. The mercury bougie is passed twice a week, and the boy has been free of vomiting for two months. He is able to take practically a normal diet with the exception of meat.

It is difficult to assess the value of bougie treatment in this case. Following upon the first use of the mercury bougie, the degree of stricture became much worse, probably as a result of

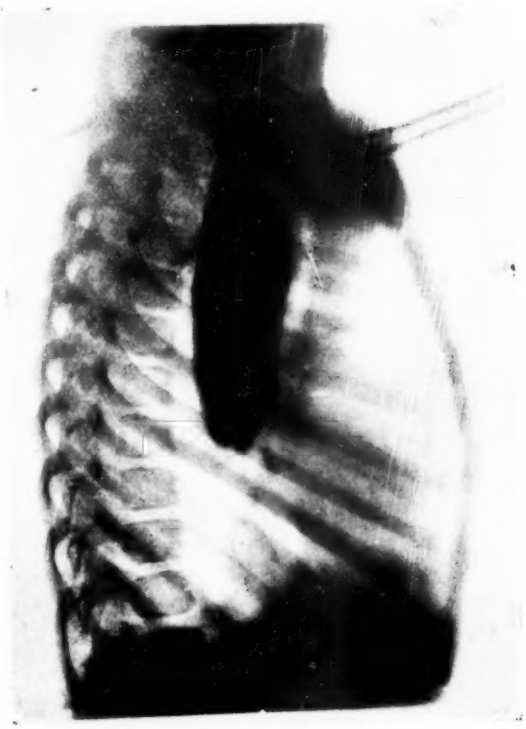

FIG. 8.

inflammatory swelling and subsequent contraction at the original site of obstruction. By keeping an ordinary small bougie permanently in situ over several weeks, the degree of contraction had been lessened, and the improvement is being maintained by the passage of a heavy mercury-filled bougie. Whether it will be possible eventually to discontinue using the bougie remains to be seen. The case illustrates some of the difficulties that may follow treatment by bougies in this condition.

Case 7. G. C., male, aged 4½ years, was admitted to hospital with a history of bouts of vomiting which had started immediately after birth. The attacks of vomiting persisted for about a week at a time, when both solids and liquids were regurgitated. The diet had consisted of fluids and semi-solids such as rice and eggs, more solid food being invariably refused.

On admission, the boy was desperately ill and extremely emaciated, weighing only 22 lb. There were no abnormal physical signs, and the Wassermann reaction was negative. X-ray examination (Fig. 7) showed an abrupt constriction in the œsophagus at the level of the 7th dorsal vertebra.

The condition of the child rapidly deteriorated, and in spite of stimulant treatment death occurred 5 days after admission. Permission for post-mortem examination was refused.

Case 8. Previously recorded by Dr. Paterson.[4]. V. B., male, was admitted to hospital for the first time at the age of 5 years, with a history of effortless vomiting after meals dating from birth. Constipation had also been a feature from birth.

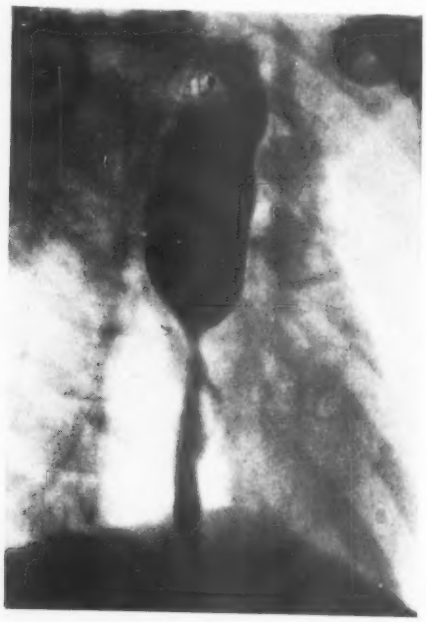

FIG. 9.

FIG. 10.

On admission the boy was very thin, weighing 21 lb. Examined under the X-ray screen, bougies were seen to curl up when seemingly well down the œsophagus. The boy was operated upon by Mr. Tyrrell Gray, who passed a bougie down the œsophagus, opened the stomach, and grasped the lower end of the bougie with forceps. The bougie was then withdrawn a little way up into the œsophagus and the lower end of the œsophagus was dilated with the forceps. No evidence of obstruction at the cardia was found during the operation.

Six months later the boy was re-admitted with a severe bout of vomiting. X-ray examination showed a constriction in the œsophagus 1½ in. above the cardia.

The child was not seen again for two years. In the meantime he had been unable to take solid food, and at times everything, including water, was returned. He was now 8 years old, and weighed 27 lb. X-ray examination (Fig. 8) again showed retention of a bismuth meal in the œsophagus well above the diaphragm at the level of the 7th thoracic vertebra. Gum elastic bougies were now occasionally passed, but without any improvement.

The patient was not seen again until he was 13 years old. His weight was then 43 lb., equivalent to the weight of a child of 6 years, and his height was 50 in. He was still subject to attacks of vomiting, but had learnt that by eating slowly, he was able to retain more food. After this lapse of 5 years, X-ray examination (Fig. 9) showed no appreciable change in the œsophagus. He was now subjected on several occasions to the passage of a heavy mercury-filled bougie, which generally entered the stomach without difficulty, but felt as though it were gripped during withdrawal. After a few weeks, his weight rose to 47 lb., and he was able to retain soft solids. It is as yet too soon to say whether this improvement will be maintained.

Fig. 11.

Case 9. C. B., male, was admitted to hospital at the age of 6 years, with a history of vomiting which dated from birth. The vomiting took place generally during a meal, and was partially controlled by limiting the diet to fluids. For several months before admission, œsophageal bougies had been passed once a week, without producing much relief.

On admission the boy weighed 33 lb. There were no abnormal physical signs. X-ray examination (Fig. 10) showed the bismuth meal held up in the œsophagus opposite the 7th thoracic vertebra. During a month in hospital, ordinary œsophageal bougies were passed occasionally, and a slight improvement was recorded.

The patient was seen again 5 years later. For four years after his discharge he had continued to vomit small amounts every day, and about once a month had had a severe bout of vomiting. The attacks had gradually lessened, and for the last year he had not vomited and was able to take solid food. An X-ray screen examination showed no delay in the passage of an opaque meal through the œsophagus.

The bougie treatment was in this case so irregular, and was abandoned so long before the boy eventually improved, that it can have played no part in the boy's recovery. The œsophageal condition would appear rather to have undergone a spontaneous cure.

Case 10. H. G., female, was admitted to hospital when 2½ years old. She was a premature baby, and had been subject since birth to attacks of vomiting after meals. Solid food was invariably returned in an unaltered condition.

On admission, her weight was 22 lb. There were no abnormal physical signs. X-ray examination on two occasions (Fig. 11) revealed an obstruction in the œsophagus at the level of the 7th thoracic vertebra. During 2 months in hospital she was given a fluid diet, on which the vomiting ceased, and she gained 2 lb. in weight.

Six months later she was re-admitted on account of a return of the vomiting. Bougies were passed down the œsophagus on three occasions, but no improvement was noticed. A fluid diet again gave the child relief from her symptoms.

Her third admission was a year later, again owing to a return of vomiting, and again she improved on a fluid diet. On her discharge, an X-ray screen examination showed no delay in the passage of an opaque meal through the œsophagus, and she was able to take such solids as bread and butter, and mashed potatoes.

The child remained in good health for a year, and then developed tuberculous meningitis. At the post-mortem examination the diagnosis of tuberculous meningitis was confirmed. The mediastinal glands were caseous, but were not attached to, nor pressing upon, the œsophagus. The œsophagus, both on its external and internal surfaces, appeared normal. No evidence could be found of constriction of the wall, nor of hypertrophy of the musculature, or ulceration of the mucosa. Microscopical examinations of the œsophagus, taken at various levels, showed nothing abnormal. The only other feature at the autopsy was the congenital absence of the left kidney and ureter.

The cause of the œsophageal obstruction in this case is difficult to determine with certainty. The likeliest explanation in our view is that the obstruction was due to a congenital narrowing of the œsophagus which, with the normal growth of the parts, gradually underwent a spontaneous cure. Our reasons for adopting this attitude are detailed at length in the discussion which follows on the first 10 cases as a group.

## Group 1: Clinical survey.

Ætiological factors.—Five of the ten preceding cases were prematurely born, one at 7 months, the other four during the 8th month. This number of premature babies forms a high proportion, but in view of the small total number of cases, one cannot draw any conclusion from this curious feature. With regard to the place in the family, four children were the outcome of first pregnancies, the remainder occupying various places in the family from the 2nd to the 5th.

There were eight boys affected to two girls, which gives a proportion almost identical with that found in such other congenital abnormalities of the alimentary tract as congenital stenosis of the pylorus, and idiopathic dilatation of the colon.

In one instance (Case 4) a paternal uncle had suffered from an exactly similar illness, which had undergone a spontaneous cure when he was 15 years old. In his case, no bougies had been passed.

The Wassermann reaction was performed in two cases, and was negative in both. Clinical evidence of syphilis could not be found in any of the cases. In only one instance (Case 10) was there evidence of tuberculosis, and, although the mediastinal glands in that child were caseous, they were not attached in any way to the œsophagus. The infectious fevers were not more frequent than might be found in any small group of children, and in most cases they

produced no effect upon the symptoms, except in Case 6. In this boy, the vomiting ceased abruptly with the onset of paratyphoid fever, and did not recur until the temperature had fallen to normal.

Symptomatology.—The symptoms arose in all cases during the first year of life. In seven instances, the vomiting, which was the first and most severe symptom, actually dated from birth. Of the remaining cases, one commenced to vomit at 10 days old, another at 6 weeks, and the third at 11 months, when weaning on to solid food was attempted. In most of those children who vomited from birth, the vomiting was noticed to become worse when solid food was introduced into the diet. The fact that the vomiting was in one case delayed until the child was weaned, and was aggravated at that time in others, is what would be expected if the œsophageal obstruction were of the nature of a congenital stricture, for such a condition would be liable to different degrees of severity in different cases. Presumably in those cases where the vomiting dated from birth, the narrowing was more pronounced than in those where this symptom was delayed until the attempt to give solid food was made.

The most prominent symptom was vomiting, which was often described as effortless, and generally occurred during or immediately after a meal. The vomited material consisted of undigested food, mucus and saliva. In some instances the vomitus was copious, and obviously consisted of more than one meal. In one child (Case 1) the vomit was reported to have been occasionally bile-stained. In most cases, a feature of the vomiting was its periodic exacerbation into a severe bout lasting up to a week, during which both solid and fluid food were returned. During the interval between such bouts, which was usually about three weeks, vomiting occurred occasionally, particularly if solid food was given. The significance of these periods of increased vomiting is uncertain; they may possibly mark an aggravation in the degree of the stricture by inflammatory swelling, with perhaps superadded spasm as the result of an attempt to force solid particles of food through the stricture. Certainly in some cases, attempts to pass œsophageal bougies gave rise later on to an increase of the symptoms, probably as a result of injury to the stricture.

The effects of such persistent vomiting appeared in the stunting and poor nutrition which were evident in all the cases. The accompanying table shows the actual amount of under-development noted, and it will be seen that in several instances the weight was not more than half the normal for the age, while the height was also below the normal standard.

Constipation was a frequent symptom, which one would expect in view of the prolonged starvation. The constipation ran parallel with the vomiting.

X-ray evidence.—X-ray examination in all these cases has demonstrated that the level of the obstruction in the œsophagus is well above the dome of the diaphragm, so that it seems clear that neither spasm of the diaphragm nor abnormalities of the cardiac sphincter can have any bearing upon the pathogenesis of the condition under discussion. In order to be certain that obstruction at the cardiac orifice would give an obviously different X-ray picture, the œsophagus of a boy who died at the age of 4 years, was ligatured just at its entry into the stomach. The œsophagus was then filled with a bismuth meal,

and an X-ray picture of the cadaver was taken. The picture showed the bismuth shadow continuing well below the level of the diaphragm, the appearance being exactly similar to that seen in adult cases of 'cardiospasm' or 'achalasia of the cardia.'

TABLE SHOWING UNDER-DEVELOPMENT IN CASES 1—10.

| Case | Age in years | Height in inches | | Weight in pounds | |
|---|---|---|---|---|---|
| | | Expected | Actual | Expected | Actual |
| 1 | 3 | 35 | 27 | 33 | 15 |
| 2 | 6½ | 46 | 44 | 46 | 40 |
| 3 | 3 | 35 | 34 | 33 | 17 |
| 4 | 2 | — | — | 28 | 14 |
| 5 | 11 | 56 | 53 | 70 | 55 |
| 6 | 5½ | 42 | 38 | 43 | 35 |
| 7 | 4½ | — | — | 39 | 22 |
| 8 | 13 | 59 | 50 | 78 | 43½ |
| 9 | 6 | — | — | 46 | 33½ |
| 10 | 4 | — | — | 37 | 24 |

The site of obstruction in our cases appears to lie approximately half-way between the level of the bifurcation of the trachea and the cardia, at the level of the seventh thoracic vertebra.

One may sometimes be misled when examining these children under the X-ray screen, because the obstruction, although great enough to prevent the passage of solid food, is not always sufficiently severe to interfere with the swallowing of fluids. This is particularly likely to be the case in children who do not vomit until towards the end of the first year, when solid food is being added to the diet. If such cases are screened while they are swallowing an opaque fluid, it may be seen to pass down the œsophagus without apparent hindrance. It is better to give the children an opaque solid to swallow, such as a bismuth biscuit, as by this means an œsophageal obstruction may be revealed when an opaque fluid has failed to do so.

Pathology.—Although the preceding ten cases form a clinical group with well-defined characteristics, it is difficult to place them on an uniform pathological basis. It may be that there is more than one morbid process concerned. The post-mortem evidence in the two cases which came to autopsy is at first sight conflicting, for while one (Case 1) showed a definite organic stricture, the other child (Case 10), who had experienced complete relief of symptoms for a year before death, showed no abnormality of the œsophagus. It is possible that if the opportunity had arisen of examining the œsophagus of Case 10 while the œsophageal symptoms were present, some evidence of abnormality would have been found.

Acquired stenosis, such as follows the swallowing of caustics, can safely be excluded since in no case was there a history of the swallowing of any irritant. In addition the level of obstruction was not that usually found in cases of stricture due to caustics.

Certain features gathered from our clinical survey seem to bear upon the pathogenesis of these cases. The onset of symptoms during the first year, often actually from birth, suggests that the œsophageal obstruction was congenital, and this view is in no way invalidated by the fact that in two instances (Cases 2 and 5) the onset of vomiting was delayed until the end of the first year. In both these children the later history showed that the degree of the stricture was insufficient to hinder the passage of fluids, and therefore it was not until solid food was taken that symptoms appeared.

Case 10 may be taken as a typical example of the whole group. Here we have an uncomplicated case consistently treated by fluid diet only, which went on to complete cure, and in which death from incidental disease rendered an examination of the œsophagus possible. The œsophagus was carefully examined, and sections at various levels were made. No evidence of stricture, hypertrophy or inflammation was found. The œsophagus in fact was absolutely normal. It will be profitable to discuss the pathogenesis of this group in the light of the evidence afforded by this case, and to illustrate the discussion by reference to the other cases where additional factors operated.

At least two possible explanations arise. These cases may be (1) examples of achalasia of the middle or lower end of the œsophagus ; or (2) the obstruction may be due to a congenital narrowing of the middle or the lower third of the œsophagus.

(1) Achalasia.—We can find no record in the literature of a case of achalasia occurring in the middle of the œsophagus, nor at the junction of the middle and lower thirds. Further, the normal condition of the œsophagus in Case 10 was most unlike the descriptions of it in cases of achalasia of the cardia, in which there is always hypertrophy and usually dilatation of the muscular wall of the œsophagus. To ascribe the cause of Case 10 to achalasia is to assume that cases of achalasia treated by fluid diet alone will undergo spontaneous cure, with the production of a normal œsophagus from one which was previously hypertrophied and dilated. Achalasia is, however, notorious for its persistence when untreated by bougies. Bougie treatment of the cases under discussion tended to aggravate the trouble. Finally, as mentioned above, all these cases commenced vomiting from birth, or as soon as any attempt to give food more solid than milk was made. Achalasia in childhood is very uncommon, but as will be shown later, when it occurs it is a disease of later childhood rather than of infancy. These considerations render it unlikely that achalasia is the cause of the obstruction in the cases of this group.

(2) Congenital abnormality.—The œsophagus has a double origin. The upper or para-tracheal part arises from the retro-pharyngeal segment of the foregut, while the lower or retro-tracheal part is developed from the pre-gastric segment of the foregut. Setting aside atresia and other fatal anomalies, congenital œsophageal obstruction at the level seen in our cases may arise in two ways. Either the junction of the two segments may be narrowed, or the lower segment in part or in whole may be narrowed, due to inadequate growth. We believe that under suitable conditions of treatment, spontaneous cure can

occur in a certain time by the growth of the œsophagus to its normal size and calibre. The length of time is uncertain, but in Case 10 cure occurred at the age of 3½ years. A study of the other cases shows that the length of time required for cure varies, and is probably adversely influenced by the forcible dilatation of the œsophagus. Such a conception accounts for the success that was obtained by treating these cases simply on a fluid diet. Had achalasia been the true explanation of these cases, bougie treatment should have given more gratifying results than were actually obtained.

The possibility of an element of spasm in several cases is suggested by the variability of the symptoms. There occurred in some of these children definite bouts of severe vomiting, with intervals of comparative freedom (Cases 1, 4, 5, 7, 9, 10). These periodic exacerbations probably depended upon a recurring spasm superimposed upon a congenital narrowing of the œsophagus. The spasm was possibly associated with injury or irritation of the œsophagus at the site of the stenosis by unsuitable or stagnant food. In Case 6, the freedom from vomiting during paratyphoid fever may have been due to the presence of a spasmodic element in the case, which was abolished during the fever.

Examples of œsophageal obstruction due to hysteria have been recorded, but the age of onset of symptoms in the cases under consideration discounts such an explanation.

It is our opinion that the cases we have described should be regarded as examples of congenital narrowing or stenosis of the œsophagus, with in some instances a secondary spasmodic element. Recovery is possibly brought about by the gradual growth of the parts, until eventually the obstruction is literally outgrown, a process which has its parallel in the gradual disappearance of the symptoms of congenital laryngeal stridor.

In 1920, Ashby[5] described a group of 5 children with symptoms similar to those of our group. In one of his examples, a boy aged 4 years who had vomited from birth, post-mortem examination showed a fibrous stricture of the œsophagus one inch above the diaphragm. Only a narrow probe could be passed through the stricture. Ashby regarded these cases as primarily spasmodic, the inflammatory stricture being a later development.

Treatment.—Various lines of treatment, by operation, bougies, and diet, have been carried out on the cases we have described. An open operation was done in one case (Case 8), but was not successful. Ordinary œsophageal bougies were passed on three children: in two no improvement took place; in the third improvement was only temporary. In addition, mercury-filled bougies were used on three cases, two of which improved, but sufficient time has not yet elapsed to say if this will be maintained: in the other child (Case 6) the use of the heavy bougie was followed by a definite contraction of the lumen of the stenosis, from which a long and arduous recovery was gradually made. Treatment by means of a prolonged fluid diet only was used consistently in four cases, three of which are cured, while the fourth was free of symptoms on discharge from hospital a few months ago. Cases 1 and 7 were at the time of admission to hospital in a very bad condition and died shortly afterwards, offering no opportunity for effective treatment.

The most satisfactory results were obtained by giving a fluid diet over a long period, possibly for two or three years. Such treatment demands great patience, but is justified by results. Attempts to effect a speedier cure by more active measures, especially by bougie treatment, are not only unlikely to be successful, but may actually aggravate the condition, and make it worse.

Greig[6] in 1921 drew attention to the clinical manifestations of congenital strictures of the œsophagus, and in urging their recognition as a clinical entity, he emphasized the value of treatment on dietetic lines alone, without the use of bougies. While our paper was in course of preparation, Beatty[7] published 57 cases of congenital stenosis of the œsophagus. His paper includes a full bibliography. He describes two varieties of congenital stenosis of the œsophagus. The first consists of a local narrowing of the lumen of the œsophagus without pathological changes in the wall, and on this latter point he distinguishes these cases from examples of acquired stenosis. The presence of pathological changes in the œsophagus at the level of the stenosis does not, however, entirely exclude the possibility that the narrowing was congenital, for as a result of trauma from the attempted passage of bougies, or from stagnation of food above the stricture, injury to the mucosa might occur and be followed by an inflammatory reaction. This would eventuate in fibrous constriction where formerly there was simply a congenital narrowing. With regard to treatment, Beatty is in agreement with Greig that a fluid diet offers the best chance of recovery.

The other variety of congenital obstruction, which has been well described by Guisez[8], consists of a thin incomplete membrane which stretches across the œsophagus. This type has been treated with success by the intentional rupture of the membrane by means of bougies or with the œsophagoscope.

In any child in whom the presence of a congenital narrowing of the œsophagus is suspected, it is essential to examine the patient by X-rays after he has swallowed an opaque, and preferably solid, meal. If by this means the diagnosis is confirmed, the next procedure should be a very careful œsophagoscopy to determine whether the stricture consists of an incomplete septum across the œsophagus, or a simple narrowing of the lumen. In the latter case, persistent treatment by a fluid diet should be instituted, and the blind passage of bougies avoided.

GROUP II. (CASES 11 AND 12.) OBSTRUCTION AT LEVEL OF DIAPHRAGM.

A study of the cases of congenital stenosis tabulated by Beatty shows that the majority occurred in the lower half of the œsophagus, some actually at the level of the diaphragm. A few were situated in the upper half. The two following cases have clinical resemblances to those we have already described, but the account of them has been delayed until now because the level of the obstruction was at a lower level in the œsophagus.

Case 11. F. W., boy aged 5 years, was admitted to hospital in 1910 with the history that he had had recurrent attacks of vomiting since birth, and that these had been accompanied by constipation.

On admission the boy weighed only 16 lb. All attempts at oral feeding gave rise to vomiting, and so recourse was made to feeding by rectal enemata. The child rapidly weakened and died. At the post-mortem examination, the œsophagus was progressively dilated and the muscle

hypertrophied down to the level of the diaphragm, where the lumen of the œsophagus was definitely narrowed, although the muscle at this point was not thicker than that of the œsophagus above.

Case 12. V. J., boy aged 3½ years, was admitted to hospital with the history that since birth (he was born prematurely at 8 months) he had had periodic bouts of vomiting, and had lived almost entirely on fluids.

On admission the child was thin, weighing 22 lb. There was extensive œdema of the face, hands and feet, and the gums were ulcerated. His condition was at first regarded as due to nephritis, which the presence of blood in the urine seemed to confirm. Renal function tests proved to be normal, and the Wassermann reaction was negative. The boy's general condition gradually improved, but periodic vomiting continued, and he failed to gain weight. He was then suspected of suffering from œsophageal obstruction, and œsophageal bougies were passed on several occasions. These met with no obstruction, but nevertheless gave temporary relief from the attacks of vomiting. X-ray examination showed that a bismuth meal passed quickly into the stomach.

The boy continued to vomit at intervals, and eventually developed a fatal broncho-pneumonia six months after his admission.

At the post-mortem examination, the œsophagus was dilated and the muscle hypertrophied. These changes commenced about an inch below the cricoid cartilage, and terminated at the diaphragm, where the œsophagus underwent a thick fibrous constriction.

### Discussion of Group II.

It will be noticed that in both these children (Cases 11 and 12) the vomiting dated from birth and occurred in bouts, being in these respects similar to the previous cases. Also at both autopsies narrowing of the œsophagus was found. It is interesting to note that in the first case, in which bougies had not been passed, narrowing of the œsophagus without fibrosis was present, while in the second case, in which bougies were used, there was a fibrous stricture.

We regard these cases as examples of congenital stenosis of the œsophagus at the level of the diaphragm.

### Cardiospasm.

Although many of the preceding cases were originally regarded as examples of cardiospasm, reasons have been given for considering them to be due to congenital stenosis of the œsophagus. The question arises whether the neuro-muscular disorders of the cardia, variously known as cardiospasm, phrenospasm, and achalasia of the cardia, which are found in adults, ever occur in infancy or childhood. Other conditions which are ascribed to neuro-muscular defects, such as Hirschsprüng's disease and idiopathic dilatation of the bladder, give rise to symptoms during infancy, so that by analogy a similar state of affairs at the lower end of the œsophagus might be expected to occur at that age. According to Hurst[9], the symptoms of achalasia of the cardia may be met with at any age.

The following case, for which we are indebted to Dr. Paterson, under whose care the child was admitted to the Westminster Hospital, is a typical example of cardiospasm. The symptoms first appeared when the patient was 8 years old.

P. R., boy aged 8½ years, was admitted to hospital with a history that for 4 months he had vomited after almost every meal. Both fluids and solids were returned. The appetite was good, but recently he had been losing weight. Previously his health had been good.

On admission, he weighed 43 lb. There were no abnormal physical signs. An X-ray examination (Fig. 12) showed an appearance typical of cardiospasm. The œsophagus can be seen dilated and filled with bismuth down to the level of the cardiac sphincter, well below the level of the dome of the diaphragm.

A No. 16 mercury-filled bougie was passed down the œsophagus, entering the stomach without difficulty. The bougie was then passed daily, and the boy made steady improvement, rapidly losing his symptoms and gaining 3 lb. in weight in the first month. He was taught to pass the bougie himself, and on discharge he was supplied with a bougie for use at home.

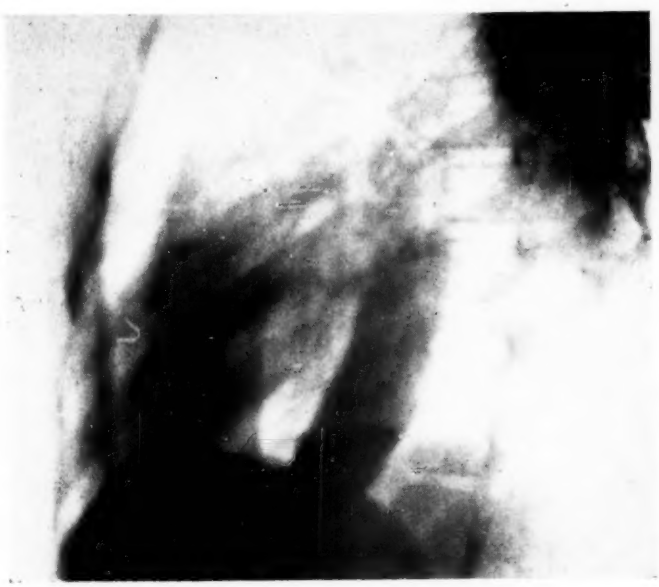

FIG. 12.

We have been able to discover very few such cases in the literature. In Rolleston's original case[10], a boy who died of cardiospasm had had symptoms since 8 years of age. Sears[11] described a boy in whom symptoms appeared at the age of 7 years. Messeloff, Shulman and Buckstein[12] recorded a typical instance in a boy who had had symptoms since the age of 10 years. These authors collected eleven cases of ' cardiospasm ' in children from the literature, but the descriptions of some of these are so incomplete that it seems uncertain whether they were really examples of cardiospasm. Thus, in the one case that came to post-mortem examination, there was found a fibrous stricture of the œsophagus 5 inches above the cardia. In six cases there was neither radiological nor post-mortem evidence to support the diagnosis. Spasm of the cardia was found in an X-ray examination of a boy aged 10 years, but the age of onset of the symptoms was not given. Of the remainder, an infant aged 10 months had had attacks of vomiting for 6 months ; X-ray examination showed a spasm of the cardia, which lasted for 30 seconds before part of the opaque meal passed on into the stomach (Méry). In describing this case, the

author considered that the cause of the spasm lay in excessive swallowing of air. Another child aged 3 years had had attacks of choking and vomiting after meals since birth; X-ray examination showed spasm at the cardia. The spasm was quickly relieved by giving atropine and benzyl benzoate (Bruce). In a third case, a boy aged 12 years had suffered from regurgitation of food from the œsophagus since 3 years old; X-ray examination showed obstruction at the cardia. The child was treated with Plummer's hydrostatic dilator (Seegar).

In the case of a boy aged 5 years reported by Castronovo[13], vomiting of food from the œsophagus had occurred since birth. The X-ray picture was exactly similar to those seen in adult cases of cardiospasm, and the author's title of 'Congenital Spasm of the Cardia' is a concise description of the case. A similar instance was described by J. A. M. Cameron[14], of a boy who died when 6 years old. This child had suffered from bouts of vomiting since the age of 6 months. At post-mortem examination, the œsophageal wall was hypertrophied, the thickest portion being at the cardia; in this respect the case differs essentially from the cases which Hurst has described as achalasia of the cardia, in which the œsophageal wall is hypertrophied down to, but not including the cardiac sphincter. We have not been able to find conclusive evidence that achalasia of the cardia occurs in infancy, although it does rarely appear in the later years of childhood. Spasmodic contraction of the cardiac sphincter does occasionally occur in infants, as evidenced by the cases of Méry, Bruce, Castronovo, and Cameron.

## Summary.

Ten examples of congenital narrowing of the œsophagus at the level of the seventh thoracic vertebra are reported, and the clinical picture of this condition is described. Treatment by persistent fluid diet is recommended, the passage of bougies being likely to do more harm than good. Two cases of congenital stenosis at the level of the diaphragm are also recorded. The question of the occurrence of spasm of the cardia and achalasia of the cardia in infancy and childhood is discussed.

We wish to express our thanks to the Medical Staff of the Hospital for Sick Children, Great Ormond Street, for their permission to make use of the hospital records.

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# REMOTE PROGNOSIS OF PNEUMONIA.

BY

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While studying the after-history of a number of patients who had been treated for pneumonia at the Children's Hospital, Birmingham, I became particularly interested in the fate of those who had suffered a prolonged pneumonia. In this group, the specific fevers and the age at which the patients suffered pneumonia, appear to have little bearing on the remote prognosis. Certain clinical features are emphasized, which a study of what I shall call ordinary pneumonia patients had led me to suspect as factors disposing to pulmonary catarrh and fibrosis.

As a background for the notes of fifty-eight patients from the Hospital for Sick Children, Gt. Ormond Street, and the Children's Hospital, Birmingham, I will describe briefly what I found in the first two hundred patients recovered for a period of from one to ten years, from pneumonia of all kinds.

It would be tedious to give in this paper all the lists and definitions with which I worked. Briefly, a pyrexial illness with cough and a lowered pulse-respiration ratio lasting more than four days, covered most cases. That the cases were representative of pneumonia in childhood may be seen from Table I, which includes judgement of type from the case records.

TABLE I.

| Length of pneumonia | No. of cases | Type of pneumonia | No. of cases |
|---|---|---|---|
| Short (less than 5 days) ... | 30 | Alveolar ... ... ... | 100 |
| Average length (5-15 days) ... | 130 | Interstitial ... ... ... | 44 |
| Prolonged (over 3 weeks) ... | 29 | Indeterminate } ... ... | 56 |
| Empyema ... ... ... | 21 | Empyema } | |

These patients were examined, and a special history was taken of measles and whooping cough, with their severity, using absence from school and confinement to bed as criteria of severity.

*Symptoms.*—Nearly half the patients were quite well at the time of examination, and had been without chest symptoms since the illness recorded. Others described cough and ill health for several months or years after their pneumonia. In many of these, the severity of the symptoms gradually declined, or they were cut short by an acute illness, sometimes by another attack of pneumonia.

TABLE 2.

| Present age | Symptoms | | | Total |
|---|---|---|---|---|
| Years. | Nil | Slight | Severe | |
| Under 6 ... ... ... | 23 | 19 | 22 | 64 |
| 6—10 ... ... ... | 17 | 17 | 12 | 46 |
| 10—16 ... ... ... | 48 | 24 | 18 | 90 |
| | 88 | 60 | 52 | 200 |

52 patients (Table 2) were found to be suffering from severe symptoms of recurrent or chronic pulmonary catarrh: they included 14 cases of well-marked fibrosis.

*Physical signs.*—Diminished expansion of one side of the chest, impairment of resonance, and poor air entry were found together in 5 per cent. of the 'no symptom' group, and in 40 per cent. of the 'severe symptom' group. Added sounds were common in the latter.

*Radiography.*—The first 125 patients who attended were X-rayed, and 101 successful chest radiograms were reported on by Dr. Black and Dr. Teall. The reports are summarized in Tables 3 and 4.

TABLE 3.

| X-ray report | Pneumonic type | |
|---|---|---|
| | Alveolar | Interstitial |
| Number of cases ... ... ... ... ... ... ... | 52 | 31 |
| Normal chests ... ... ... ... ... ... ... | 15 | 2 |
| Generalized increase of striæ density ... ... ... | 19 | 23 |
| Localized striæ increase and localized fibrosis ... ... | 18 | 12 |

A consideration of the figures shown in Table 3 suggests that (*a*) an interstitial pneumonia leaves a generalized increase of peribronchial tissue in a large proportion of cases (Fig. 1); and (*b*) the frequency of scarring is far less after alveolar pneumonia.

TABLE 4.

| X-ray report | Present symptoms | | |
|---|---|---|---|
| | Nil | Slight | Severe |
| No of cases ... ... ... ... ... ... | 49 | 29 | 33 |
| Normal ... ... ... ... ... ... | 15 | 6 | 4 |
| Generalized striæ increase ... ... ... ... | 24 | 17 | 23 |
| Localized striæ increase and fibrosis ... ... | 11 | 7 | 11 |

Table 4 shows that (*a*) those patients who now present slight symptoms or none at all, show five times as many normal radiograms as those patients who suffer severe symptoms of pulmonary catarrh; and (*b*) a considerable amount of scarring may be present in a chest after pneumonia, although the patient has no symptoms (Fig. 2).

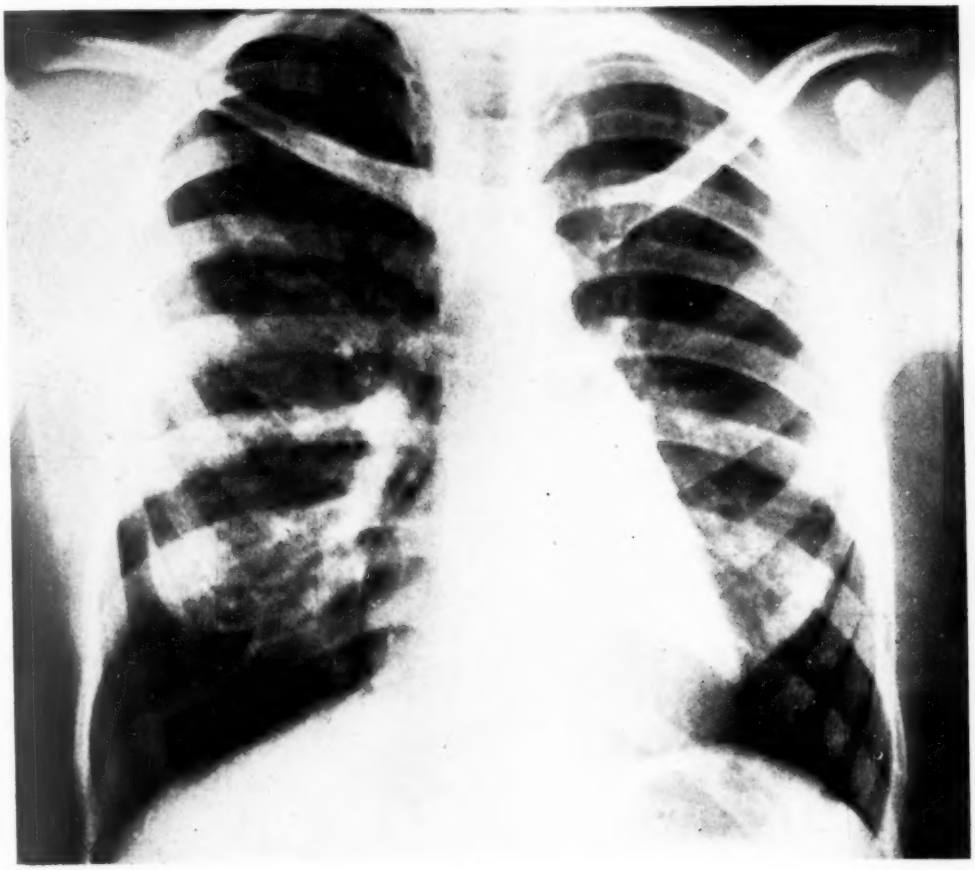

FIG. 1.

Fig. 1. F. A. $11\frac{8}{12}$ yr. Pulmonary fibrosis with severe symptoms. Primary pneumonia at 6 months and at 2 years lasting 6 days. Has had measles, not whooping cough. Skiagram showing increase in striae density, especially right side and to base.

It has been already stated that 14 patients were found to show well-marked pulmonary fibrosis. Is this lesion due to the pneumonia, for we know that a catarrhal attack in a lung so damaged will simulate pneumonia? Pneumonia secondary to measles or whooping cough is an accredited cause of fibrosis, but a detailed enquiry for the specific fevers left 20 patients with severe symptoms for which those could not be held responsible. These 20 patients had either not suffered from measles or whooping cough, or had had a mild attack of measles only. 14 of them reported two or more attacks of pneumonia,

whereas of 20 patients who had suffered measles or whooping cough with evidence of severe pulmonary complications, seven only, reported more than one attack of pneumonia.

Patients who recover from pneumonia before three years old would appear to have the same after history as children who have pneumonia later (Table 5).

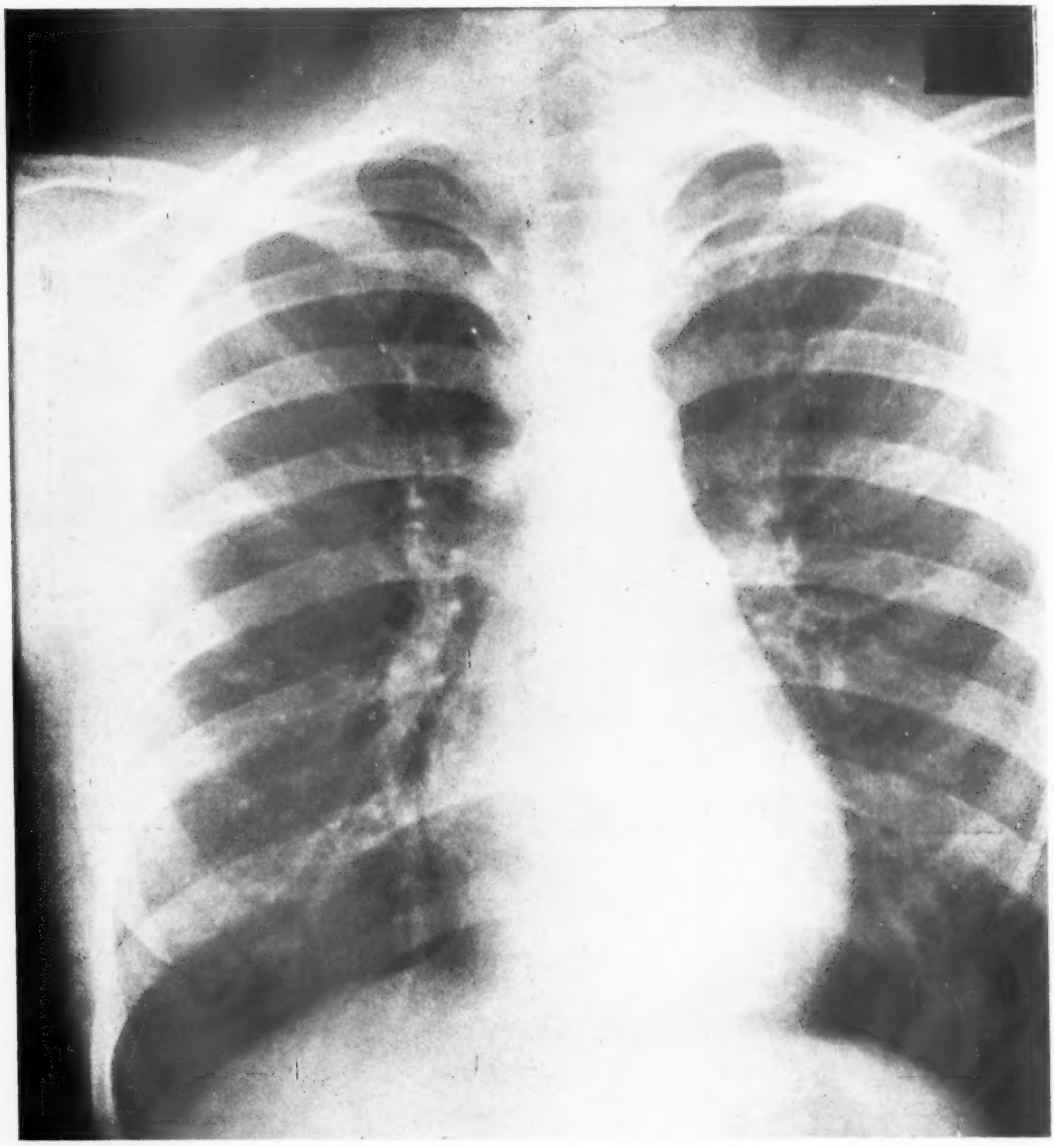

FIG. 2.

Fig. 2. L.S., 13 yr. No symptoms. Had pneumonia at 12 months and at 3 years. Skiagram showing generalized increase in striæ with basal spread.

TABLE 5.

| Age at pneumonia | No. of cases | Severe symptoms |
|---|---|---|
| Under 3 years ... ... | 96 | 25 |
| Over 3 years ... ... | 104 | 27 |

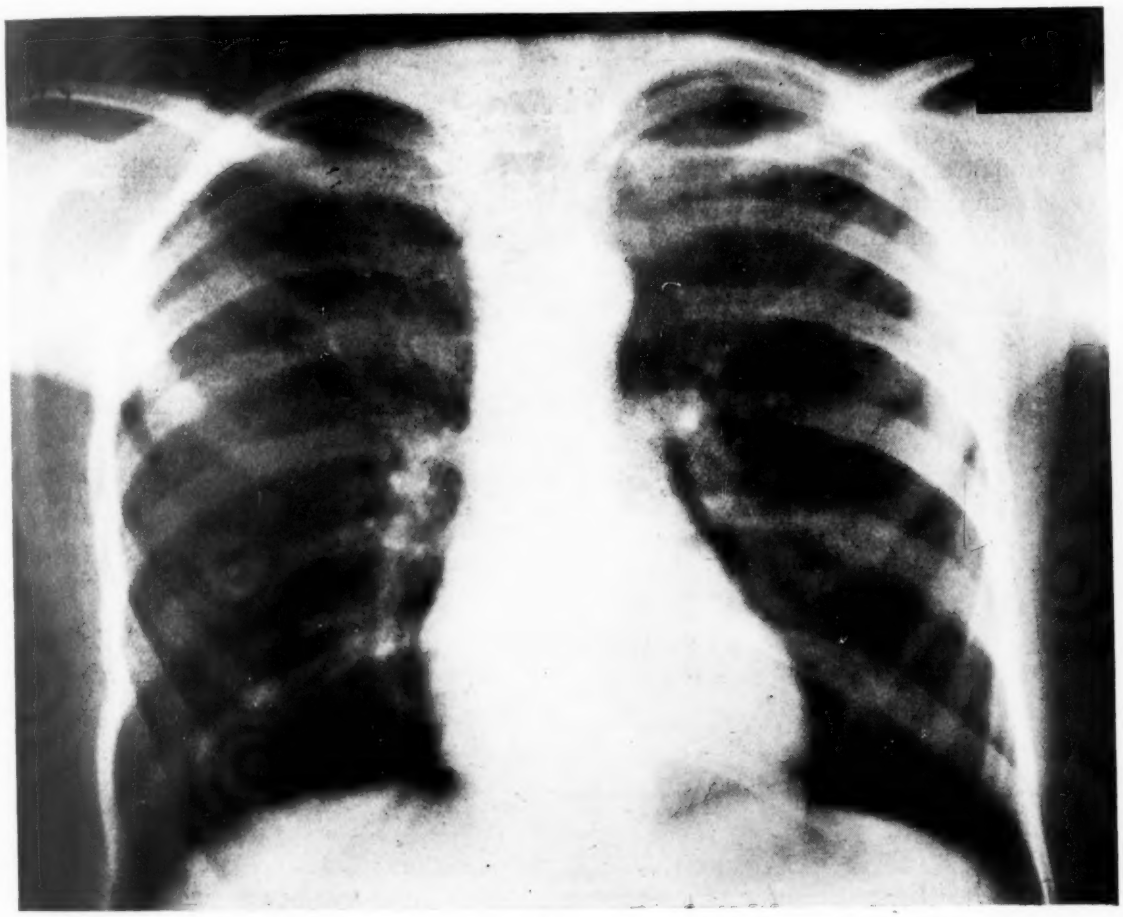

FIG. 3.

G. C., 11½ yr. Radiological report, practically normal.

The effect of pneumonic type on the remote prognosis will depend on my judgment from a study of the case records. This was made before the patients were examined, and I have used Professor McNeil's terms of alveolar and interstitial pneumonia for the more usual ones of lobar, primary broncho-pneumonia, and secondary broncho-pneumonia. His clinical criteria were closely followed.

TABLE 6.

| Type | Total | Severe symptoms |
|---|---|---|
| Alveolar ... ... ... ... ... | 100 | 25 |
| Interstitial ... ... ... ... ... | 44 | 16 |
| Indeterminate and empyema ... ... | 56 | 11 |

### The Remote prognosis of prolonged pneumonia.

Patients were written to who had been treated during the last ten years for a pneumonia lasting more than three weeks at the Hospital for Sick Children, Great Ormond Street, London, and the Children's Hospital, Birmingham. 58 attended for examination, and of these, one-third were found to be without symptoms, and one-third to be suffering severe symptoms of pulmonary catarrh. When we consider the cause of these symptoms, measles and whooping cough can be recognized and set aside, for the proportion of complete recoveries from the specific pneumonias is nearly the same as the average (33 per cent.). The division at three weeks was arbitrary, and purposed to find out the effect of the duration of inflammation on the lung. Tables are appended showing the type of pneumonia, the ages of the patients, and their present symptoms and signs.

*Present physical signs.*—Three of the patients without symptoms showed diminished expansion, impaired resonance and weaker breath sounds over the lower lobe of the lung principally affected by the old pneumonia (E.D., G.B., and K.A.). Two showed impaired resonance and faint breath sounds only over the same lung (E.G. and W.C.).

*Radiography.*—Thirty-three patients were X-rayed independently of the clinical examination and history. Reports were made by Dr. Shires, Dr. Black and Dr. Teall (Table 7).

TABLE 7. X-ray Results.

| Report | Symptoms absent or slight | Symptoms severe |
|---|---|---|
| Local fibrosis ... ... ... ... ... | 3 | 9 |
| Generalized striæ increase ... ... ... | 4 | 3 |
| Normal ... ... ... ... ... | 9 | 2 |

These reports correspond closely with the physical signs in only one-half of the cases in the second group (viz., J.N., L.H., A.D., V.C., R.R., and F.G.).

### Discussion.

It is difficult to escape the conclusion that the long illness in the past is closely associated with, if it is not the actual cause of, the severe symptoms of pulmonary catarrh from which 18 patients now suffer. At the same time I was

impressed by the fact that 40 out of 58 children made recoveries comparable with those 74 per cent. of the previous group which included pneumonia of all kinds. A striking coincidence, or finger post, whichever it is, is marked by the fate of those children whose prolonged pneumonia had an acute onset with evidence of early pleurisy (Table 8).

TABLE 8.

| Initials | Age at pn. | Duration | Symptoms | X-ray |
|---|---|---|---|---|
| N.Y. | 3½ | 3½ weeks | Some cgh. at 6 months intervals. | |
| F.H. | 1 1/12 | 4+ ,, | Winter cgh., no bed. | |
| N.T. | 2¼ | 6 ,, | Frequent colds and cgh., better since tonsillectomy. | F.R. |
| S.N. | 3¾ | 3+ ,, | Occ. cgh., asthma, no bed. | F.L. |
| E.G. | 4 | 8+ ,, | nil | Norm. |
| L.G. | 2 | 8 ,, | nil | F.R. |
| A.P. | 1¼ | 5 ,, | nil | |
| G.W. | 9 | 5 ,, | nil | |

Not one of the 8 patients in Table 8 is now suffering from severe symptoms, and this does not apparently depend entirely on the absence of a lung scar, unless one is to ignore the radiograms. During the examinations, evidence accumulated that two factors were of almost equal importance in the production of symptoms: first, the lung scar; and secondly, periodic infections from the upper respiratory tract. It seemed over and over again that both were necessary for the production of severe symptoms of chronic or recurrent pulmonary catarrh.

In such a small series any statistical arrangement can hardly be taken seriously, but the figures shown in Table 9 confirm what we know already, and emphasize the 'plural' pneumonias as a cause of mischief.

TABLE 9. SYMPTOMS.

| | Cases | Nil | Slight | Severe | % Severe symptoms |
|---|---|---|---|---|---|
| Total ... ... ... ... ... | 58 | 20 | 20 | 18 | 31% |
| Chronic interstitial pn. Pneumonia with rickets ... ... ... | 16 | 3 | 5 | 8 | 50% |
| Acute non-specific pn. ... ... | 23 | 10 | 9 | 4 | 21% |
| Pn. secondary to m. or wh. c. ... | 12 | 4 | 5 | 3 | 25% |
| Hist. of sev. m. or wh. c. ... | 22 | 8 | 6 | 8 | 36% |
| Hist. of two or more attacks of pn.... | 23 | 3 | 8 | 12 | 52% |
| Pn. lasting 8 weeks or longer ... | 21 | 7 | 7 | 7 | 33% |
| Pn. under 2 yrs. ... ... ... | 20 | 8 | 5 | 7 | 34% |

| Initials | No. of attacks | Age in years | Age at pn. | Pneumonia | | Duration in weeks | Present symptoms |
|---|---|---|---|---|---|---|---|
| | | | | Type | Site | | Without symptoms |
| G.B. | 1 | 8½ | 1½ | Acute ... | General ... | 4½ | Nil |
| E.D. | 1 | 7½ | 3 | ? ... ... | R.L.L., R.M.L. | 6+ | Nil |
| K.R. | 2 | 8½ | 4 | Acute ... | Gen. esp. R. ... | ? | Nil |
| T.C. | 1 | 4½ | 11/12 | Acute ... | Right ... ... | 4 | Nil |
| E.G. | 1 | 8½ | 4 | Acute ... | Left ... ... | 8+ | Nil |
| W.C. | 1 | 5 | 2 | Acute ... | Both esp. R. | 7 | Nil |
| E.B. | 1 | 11¾ | 2½ | ? ... ... | ? ... ... | 4+ | Nil |
| M.M. | 1 | 7 | 6½ | ? ... ... | R.L.L. ... | 3½ | Nil |
| R.C. | 1 | 4½ | 1¼ | Spec. wh. ... | Esp. R.U.L. ... | 8 | Nil |
| R.D. | 1 | 7½ | 6 | ? ... ... | R.L.L. ... | 5+ | Nil |
| A.G. | 1 | 8¾ | 3½ | Acute ... | Left ... ... | 3½ | Nil |
| O.S. | 1 | 10 | 11/12 | Chronic ... | ? ... ... | 3 | Nil |
| G.H. | 2 | 4¼ | 1¾ | Chronic ... | General ... | 7 | Nil |
| E.F. | 1 | 10½ | 7 | Acute recurrent | Gen. esp. L. ... | 8 | Nil |
| W.M.C. | 1 | 3¼ | 1½ | Acute ... ... | Both ... ... | 4½ | Nil |
| M.H. | 1 | 7½ | 1½ | Acute ... | Gen. esp. L. | 9 | Nil |
| A.P. | 1 | 7¾ | 1¼ | Acute ... | General ... | 5 | Nil |
| G.W. | 1 | 13 | 9 | Chronic ... | L.L.L. ... | 5 | Nil |
| W.H. | 1 | 7½ | 5¼ | Spec. m. ... | General ... | ? | Nil |
| L.G. | 2 | 4 | 2 | Acute ... | Right ... ... | 8 | Nil |
| | | | | | | | Slight symptoms. |
| E.B. | 3 | 8 | 2¼ | Chronic ... | General ... | 8+ | Winter c. no bed, not away from school ... ... ... ... |
| F.H. | 2 | 6½ | 2 | Acute ... | L.U.L., L.L.L. | 3+ | Winter c. away from school, no bed |
| T.B. | 2 | 10¼ | 2¾ | Acute strepto-coccal septi-cæmia. | Gen. esp. R. ... | 10 | Frequent cz. winter c. no bed: not away from school ... ... |
| E.B. | 1 | 6 | 1½ | Acute ... | L.U.L. ... | 3 | Past symptoms: none since T. & A. op. 1927 ... ... ... |
| V.J. | 2 | 9¼ | 3¼ | ? ... ... | L.L.L. ... | 9 | Spring cough, away school 14 days, bed 3 days ... ... ... |
| R.R. | 1 | 7 | 2¼ | Chronic ... | General ... | 9 | Winter cough (dry) ... ... |
| E.C. | 3 | 7 | 1 | Acute Rickets | Gen. esp. L. ... | 4 | Cough s. & w. not confined to bed or away from school ... ... |
| S.J. | 1 | 11 | 1½ | Spec. wh. c. ... | R. predom. ... | 6+ | Slight occasional c. ... ... |
| E.B. | 1 | 11½ | 2 | Acute ... | Both ... ... | 4½ | Cough now for first time since pn.... |
| K.E. | 1 | 7½ | 2¼ | Chronic ... | Left ... ... | 10 | Slight winter cough ... ... |
| N.Y. | 2 | 12 | 3½ | Acute ... | ? ... ... | 3½ | Cough at intervals of six months ... |
| A.A. | 1 | 11¼ | 5 | Spec. wh. c. ... | R.U.L. ... | 4 | Spring c. after cz. bed 2 days ... |
| F.H. | 1 | 10½ | 2 | Acute ... | Ph. mig. rans... | 4½ | Slight c. in w., not away from school |
| L.M. | 1 | 16 | 11 | Acute ... | Right ... ... | 3 | Slight c. at night. No exacerbations |
| G.N. | 2 | 6¼ | 3½ | Acute ... | Left ... ... | 3+ | Occas. c., worse in w., no bed; not away from school, ? asthma |
| I.R. | 1 | 8 | 1¾ | Spec. m. ... | Gen. esp. L. | 20 | Slight c. and spit: worse in w., bed day or two improving ... ... |
| E.S. | 1 | 2½ | ¾ | Acute ... | Right ... ... | 8 | Slight morning c. since wh. cough... |
| H.S. | 1 | 6½ | 4¼ | Chronic ... | R.L.L. ... | 3 | Occas. c. in w. after cz., bed a day or two ... ... ... ... |
| N.T. | 2 | 6¼ | 2¼ | Acute ... | R.U., M. & L.L. | 6 | Frequent cz. and c. before measles: improving ... ... ... |
| A.W. | 1 | 6 | 2 | Spec. m. ... | Gen. esp. R. ... | 6 | Slight cough only ... ... ... |

PHYSICAL SIGNS.

| Dimd. expansion | Impaired resonance | Breath sounds | Added sounds | X-ray report |
|---|---|---|---|---|
| Lag. R. ... | R.L.L. ... | Weak R.L.L. ... | Nil ... ... | — |
| R. lower ... | R. base ... | Weak R. ... | Nil ... ... | F. gen. |
| Lag. R. ... | R. base ... | Weak R. ... ... | Nil ... ... | — |
| L.U.L. ... | Nil ... ... | Weak L.U.L. ... | Nil ... ... | F. gen. |
| Nil ... ... | L.L.L. ... | Weak L. ... ... | Nil ... ... | Normal |
| Nil ... ... | R. base ... | Weak R. base ... | Nil ... ... | F. gen. |
| Nil ... ... | R. base ... | Equal ... ... | Nil ... ... | F. gen. |
| Nil ... ... | R. base ... | Equal ... ... | Nil ... ... | Normal |
| Nil ... ... | L. base ... | Equal ... ... | Nil ... ... | L.F. |
| Nil ... ... | R.L.L. ... | Equal ... ... | Nil ... ... | F. gen. |
| R. ... ... | Nil ... ... | Equal ... ... | Nil ... ... | Normal |
| Nil ... ... | Nil ... ... | Equal ... ... | Nil ... ... | F. gen. |
| Nil ... ... | Nil ... ... | Equal ... ... | Nil ... ... | F. gen. |
| Nil ... ... | Nil ... ... | Equal ... ... | Nil ... ... | — |
| Nil ... ... | Nil ... ... | Equal ... ... | Nil ... ... | — |
| Nil ... ... | Nil ... ... | Equal ... ... | Nil ... ... | Normal |
| Nil ... ... | Nil ... ... | Equal ... ... | Nil ... ... | — |
| Nil ... ... | Nil ... ... | Equal ... ... | Nil ... ... | — |
| Nil ... ... | Nil ... ... | Equal ... ... | Nil ... ... | S. and R. |
| Nil ... ... | Nil ... ... | Equal ... ... | Nil ... ... | F.R. |
| Both ... ... | Nil ... ... | Dim. bases ... | Gen. rhonchi. ... | — |
| L. ... ... | L.L.L. ... | Bronchial L. ... | L.L.L. ... ... | — |
| Nil ... ... | R.L.L. ... | Expn. prolonged... | Scattered ... | F. gen. |
| L. lower ... | Nil ... ... | Equal ... ... | Nil ... ... | — |
| Nil ... ... | L. base ... | Dim. bases ... | Nil ... ... | — |
| Nil ... ... | L. base ... | Faint L. base ... | Nil ... ... | F. gen. |
| Scoliosis ... | L.L.L. ... | — | Nil ... ... | Normal |
| Nil ... ... | Nil ... ... | Equal ... ... | Both L.L. ... | Gen. |
| Nil ... ... | Nil ... ... | Equal ... ... | Gen. rhonchi. ... | — |
| Nil ... ... | Nil ... ... | Equal ... ... | R. base ... ... | F. gen. |
| Nil ... ... | Nil ... ... | Equal ... ... | R.L.L. ... ... | F. gen. |
| Nil ... ... | Nil ... ... | Equal ... ... | Nil ... ... | Normal |
| Nil ... ... | Nil ... ... | Equal ... ... | Nil ... ... | — |
| Nil ... ... | Nil ... ... | Equal ... ... | Nil ... ... | — |
| Nil ... ... | Nil ... ... | Equal ... ... | Nil ... ... | — |
| Nil ... ... | Nil ... ... | Equal ... ... | Nil ... ... | F. gen. |
| Nil ... ... | Nil ... ... | Equal ... ... | Nil ... ... | — |
| Nil ... ... | Nil ... ... | Equal ... ... | Nil ... ... | Normal |
| Nil ... ... | Nil ... ... | Equal ... ... | Nil ... ... | F.R. |
| Nil ... ... | Nil ... ... | Equal ... ... | Nil ... ... | Normal |

TABLE

| Initials | No. of attacks | Age in years | Age at pn. | Pneumonia | | Duration in weeks | Present symptoms |
|---|---|---|---|---|---|---|---|
| | | | | Type | Site | | |
| | | | | | | | Severe symptoms |
| L.H. | 3 | 4 | 2½ | Chronic ... | Both esp. L. | 5+ | C. and spit s. and w. getting worse (bronchiectasis) ... ... |
| F.G. | 3 | 8½ | ¼ | Acute ... | Gen. esp. R. ... | 3 | C. s. & w., worse in w., not much bed |
| L.R. | 1 | 5½ | 4 | Chronic ... | R. ... ... | 3+ | Winter c. keeping pt. in bed ... |
| H.F. | 1 | 13½ | 4 | Spec. m. ... | Left ... ... | 4+ | C. and spit s. and w., away school 4 weeks at a time ... ... |
| R.R. | 1 | 10 | 5 | ? ... ... | Both esp. R. | 4 | Sev. w. cough (well-marked bronchiectasis) bed ... ... ... |
| V.C. | 3 | 7¾ | 5 | ? Chronic ... | L.U.L., L.L.L. | 8 | C. s. and w., worse in w., bed 14 days, several times a year ... |
| A.D. | 1 | 4¾ | 11/12 | C. rickets ... | R.U.L., R.L.L. | 8+ | Innumerable crippling attacks of cough and spit. ... ... |
| J.N. | 2 | 6½ | 2 | C. rickets ... | R.U.L., R.M.L. | 4 | Frequent c., worse in w. and now |
| S.H. | 2 | 5½ | 1½ | Acute ... | Gen. esp. R. ... | 12 | Cough s. and w. worse in w., bed 1—2 weeks ... ... ... |
| F.N. | 2 | 5¼ | 1 | C. rickets ... | Gen. esp. L. | 12 | Bad c. s and w. since wh. c. not before ... ... ... ... |
| J.C. | 2 | 4½ | 2¼ | C. rickets ... | R. than L. ... | 8 | C. s. and w. worse in w., fever and bed a day or two ... ... |
| R.W. | 4 | 4¾ | 1¾ | Chronic ... | L.L.L. ... | 3 | Cough each w. bed 2—3 weeks ... |
| D.W. | 1 | 9 | 5 | Acute ... | R.L.L. ... | 4 | Winter cough, bed a week with fever, occasionally ... ... |
| I.P. | 13 | 9½ | 1¾ | Spec. wh. ... | General ... | 6+ | C. at intervals worse in morning and in s., bed 3 days, loses much time from school ... ... |
| V.S. | 1 | 6½ | 2¼ | (Influenzal) Acute ... | Both L.L. ... | 3 | Freq. cz. and ottorrhœa since pn. cough follows cz. s and w., not much bed ... ... ... |
| M.R. | 2 | 11½ | 2 | Acute ... | R. ... ... | 4 | Cough s. and w. worse in w. short. of breath (congen. morbus cordis) |
| H.G. | 2 | 3 | 2 | ? ... ... | Gen. esp. L. | 6 | Sev. winter c., confining to house |
| V.W. | 2 | 5 | 2¼ | Spec. wh. c. ... | Gen. esp. R. ... | 11 | C. s. and w., bed 14 days in exacerbations ... ... ... ... |

Abbreviations and

All pneumonias, complicating measles or whooping cough, are marked specific m. or wh.
Under X-ray report :—
F = fibrosis.
F. gen includes reports of peribronchial thickening.

*contd.*

| Physical signs | | | | |
|---|---|---|---|---|
| Dimd. expansion | Impaired resonance | Breath sounds | Added sounds | X-ray report |
| | | | | |
| L. ... ... | Dullness L.L.L. | Bronchial L. ... | Crepitant L.L.L. | F.L. |
| Nil ... ... | R.L.L. ... | — | R. base ... ... | Bronchiectasis, R.L.L. |
| R. ... ... | Nil ... ... | Altered R. base | Right ... ... | F. bases |
| L. ... ... | L.L.L. ... | — ... | Nil ... ... | F. gen. |
| L. lower ... | Nil ... ... | Dim. L. ... ... | Crepitant L.L.L. | F.L. base |
| L. ... ... | L.L.L. ... | Bronchial L. ... | L. base ... ... | F. gen. |
| R. upper ... | R.U.L. ... | Equal ... ... | R.U.L. ... ... | F. gen. |
| R. ... ... | R.L.L. ... | Equal ... ... | L.L.L. ... ... | F. bases |
| L. ... ... | L.U.L. ... | Equal ... ... | Nil ... ... | F.L. |
| Nil ... ... | Nil ... ... | Equal ... ... | Scattered ... | F. gen. |
| Nil ... ... | L.U.L. ... | Equal ... ... | Nil ... ... | F.R. |
| Nil ... ... | L. base ... | Equal ... ... | Nil ... ... | Normal |
| Nil ... ... | Nil ... ... | Equal ... ... | Nil ... ... | E.R.L.L. |
| Nil ... ... | Nil ... ... | Equal ... ... | Nil ..... ... | — |
| Nil ... ... | Nil ... ... | Equal ... ... | Nil ... ... | — |
| Lag R. ... | Nil ... ... | Equal ... ... | Nil ... ... | Normal |
| Nil ... ... | R.L.L. ... | Equal ... ... | Nil ... ... | — |
| Nil ... ... | L.L.L. ... | Equal ... ... | L.L.L. ... ... | — |

Explanations.

Under Symptoms :—

C.=cough.

S. & w.=summer and winter respectively.

Cz.=coryza.

H.=confined to house.

A history of catarrhal attacks in infancy, and of severe measles or whooping cough was common in the third group but was not prominent. The pneumonias before two years did not crowd into that group as might have been expected.

## Conclusion.

From these observations it may be suggested that emphasis is to be placed on the amount, duration and recurrence of the interstial inflammation, in estimating the remote prognosis of pneumonia. Second or third attacks, and the occurrence or persistence of upper respiratory infections are particularly liable to cripple a child who has once suffered from this disease.

I am indebted to the physicians and radiologists at both hospitals for permission to examine their cases, and publish these results.

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# A CASE OF COARCTATION OF THE AORTA

BY

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Cases of coarctation of the aorta are sufficiently rare to be worthy of record. No systematic account of the condition is included here as the paper recently published by Poynton and Sheldon[1] mentions the chief references and gives an adequate review of the subject.

In November, 1928, a little girl of five years, the third of a healthy family of 4 children, was sent to one of us (A. P. T.), at the out-patient department of the Children's Hospital, Birmingham, by Dr. J. H. Wright of Four Oaks for an opinion on the significance of a cardiac murmur which he had discovered a few days previously when she had a cold. She was a thin, active and ill-developed child, weighing only 31 lb., the average weight of a girl of three, but nevertheless she had always been regarded by her mother as perfectly healthy, 'like the others,' though admittedly 'on the small side.'

On examination the heart was found to be a little enlarged to the left with a rather diffuse and forcible apex beat in the 5th space, 2½ in. from the midsternal line. A blowing systolic bruit was audible all over the præcordia but most marked at the base, and was conducted up into the vessels of the neck, being loudest over the left common carotid artery. A loud systolic murmur was also heard at the back in the interscapular region, and was there most pronounced in the right paravertebral area at the level of the angle of the scapula. At times the bruit appeared very prolonged, but it was never definitely biphasic; the second heart sound was clearly heard at all areas and was a little accentuated at the base.

A diagnosis of some form of congenital mal-development of the heart, probably of the type of subaortic stenosis, seemed to be satisfactory until a curious difference in the hands was noticed: the left as far as the wrist was uniformly dusky, blue and congested, and presented a striking contrast with the normal right. The difference in the appearance of the hands persisted in all positions and was, in fact, most marked when they were held above the head, for then the right became pallid and no change in the cyanotic condition of the left was observed. The hands and arms were perfectly symmetrical; there was neither œdema nor paresis in the left, and in the absence of any evidence of venous obstruction it seemed probable that the circulatory stasis on the left side was due to some interference with the arterial flow. The fact that the left brachial pulse seemed to be of smaller volume than the right supported this hypothesis and it was possible to hazard the suggestion, which subsequently proved correct, that the child had a coarctation of the aorta extensive enough to involve the origin of the left subclavian artery.

After admission to the hospital for further investigation the results of the examination in the out-patient room were confirmed; in addition, the pulsation in the femoral arteries, though undoubtedly present, was found to be distinctly feeble when compared with that in a child of like development. No sign of a superficial collateral circulation was discovered, but there was no palpable pulsation in the abdominal aorta although the patient was thin and put up with examination placidly. The brachial arteries were very prominent and appeared to be thickened. Mr. E. B. Alabaster examined the retinæ and found the arteries there small and inclined to be tortuous. The appearance of the feet and legs was normal and nothing of note was found in the other systems on physical examination.

An X-ray of the chest by Dr. C. G. Teall showed generalized enlargement of the heart of moderate degree, but no abnormality of the great vessels. An electrocardiograph by Dr. K. D. Wilkinson was normal, apart from slight indications of the changes usually associated with left-sided preponderance.

The most striking new facts elicited by examination in the wards, however, related to the blood pressure. In both arms the tension was found to be much increased, but on the left side it was nearly always slightly higher than on the right. Daily observations at the same hour were made over a period of a fortnight. On the left side the systolic pressures varied from 220 mm. to 200 mm., and the diastolic from 190 mm. to 160 mm., closely following the systolic pressure; the pulse pressure averaged only between 30 and 35 mm. In the right arm the systolic pressure varied between 215 mm. and 175mm., and the diastolic between 145 mm. and 120 mm., (the high reading was an exceptional one and the diastolic pressure was usually constant at about 130 mm. and did not follow the variations of the systolic pressure as it did on the opposite side); the pulse pressure in the right arm was commonly about 60 mm., roughly double that in the left. In making these observations it was noticed that the 'systolic bang' was much fainter and shorter on the left side. The pressure in the popliteal arteries was found to be fairly constant and equal on the two sides at 125 mm.; it was not possible to determine the diastolic levels in this situation, as no sound could be heard through the stethoscope.

The urine contained a distinct haze of albumen, but the deposit was not abnormal; the blood urea was 49 mgrm. per 100 c.cm. and the non-protein nitrogen was 46 mgrm.

As the blood pressure had been found to be very high in the arms alone and not more than slightly raised in the legs, it appeared unlikely that chronic nephritis could have contributed to the hyperpiesis in any way, but it was thought best to estimate the ability of the kidneys to concentrate urea. The methods of Calvert and Maclean were both employed; with the former the urea concentration seemed decidedly deficient; but with the latter it was found to be unusually good. Three months later after an acute intercurrent illness and shortly before death the Calvert test showed a still more diminished range, although the blood chemistry remained normal and the urine showed only a trace of albumen. In this case, in view of the post-mortem findings, it is clear that this method of estimation of renal efficiency gave a much better result than that of Maclean.

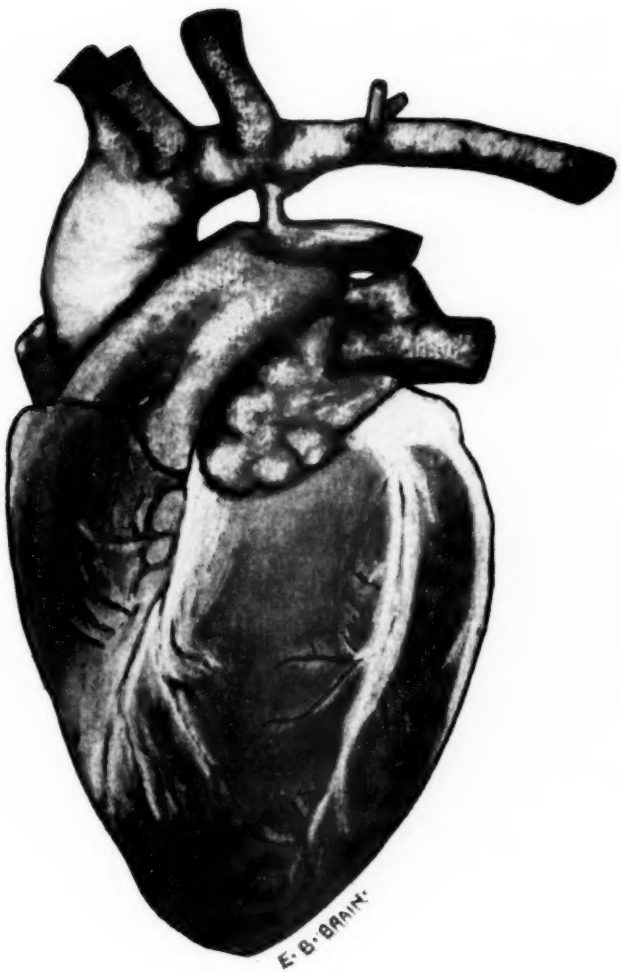
The child was discharged from hospital on November 20th, 1928, and was kept under observation as an out-patient for two months. During this period no material change in her condition was noticed.

On February 1st, 1929, she was re-admitted with lobar pneumonia at the right base. After five critical days she recovered and was about to be discharged early in March, when she developed acute tonsillitis, followed by cervical adenitis from which she rallied very slowly. Swabs from her throat showed no Klebs-Löffler bacilli. Eventually at her parents' request, though still far from well, she was allowed to go home on April 12th, 1929.

During the acute period of her attack of pneumonia several observations on the blood pressure in the brachial arteries were made and it was found that the level had fallen considerably in both, to about 150 mm. systolic and 130 mm. diastolic: curiously enough the constant difference noticed two months earlier (when the pressure in the left arm was consistently higher) did not persist and often a higher pressure was found on the right side. A few days later, however, after the crisis, the blood pressure rose to about 180 mm. systolic and during the week before she finally left hospital it had returned approximately to 200 mm. systolic, and was often above this on both sides: at this time the pressure on the left side was usually distinctly the higher by 10 or 15 mm., as it had been previously.

The marked difference in the appearance of the hands which first drew attention to the child was hardly noticeable while she was acutely ill, possibly on account of general cyanosis, though this explanation seemed rather inadequate at the time. For some weeks before she left the hospital, however, the original condition was restored and she was known in the ward as 'the child with the blue left hand.'

During this prolonged stay in hospital the condition of her brachial arteries and of those in the fundus became worse and clinically they appeared markedly sclerotic: in addition her


E·B·BRAIN·

mental condition at times was peculiar, and occasionally she vomited. The child, for no apparent reason, suffered from attacks of temper and sometimes from extreme depression: in general she was mentally dull and lethargic.

These symptoms probably were a consequence either of cerebral arteriosclerosis or hypertension, for blood and urine analyses seemed to exclude any possibility of uræmia. Repeated estimations of the blood urea, non-protein nitrogen, calcium and phosphorus were normal, but as already recorded, Calvert's test, which three months previously had given a result indicating renal impairment, now showed a very limited range. The urine remained normal apart from slight albuminuria and was passed in good quantity.

A few days after she left the hospital the child died suddenly at home. Consent to a post-mortem examination was only obtained with difficulty and unfortunately it had to be strictly limited in scope. It was carried out in a small cottage in unsuitable and difficult conditions.

The body was very emaciated (the child had vomited frequently after leaving the hospital) and on opening the thorax the lower lobe of the right lung was found to be firmly adherent to the chest wall: small quantities of fibrino-purulent material were found in the interstices of the adhesions, but there was no empyema. The heart was removed intact with the arch and part of the descending aorta, and one femoral artery and a part of the left brachial artery were dissected out. The abdominal viscera, with the exception of the kidneys, appeared normal. Permission to open the head was refused.

### Description of the Specimens.

The obvious enlargement of the heart is mainly due to cone-shaped hypertrophy of the left ventricle which forms at least three-quarters of the whole of the anterior surface. So far as could be determined by examination through windows cut in the vessels, there was no abnormality in the arterial valves of the heart, which was not very thoroughly explored in order that its value as a museum specimen might be maintained. The ascending aorta is dilated and has the shiny appearance associated with thickening of the outer fibrous coat: the innominate, left carotid and left subclavian arteries arise in their usual situations from the aortic arch, and the walls of all of them are thickened. Almost opposite to the origin of the left subclavian artery the ductus arteriosus joins the arch; it is less than a $\frac{1}{4}$-in. in length and is not patent. A little above this point, and for a considerable distance below it, the aorta is greatly constricted but nowhere obliterated: the stenosis is most marked at a point $\frac{3}{8}$-inch below the left subclavian artery where two small thickened vessels (probably the superior intercostals) take their origin. Below this point the aorta dilates a little, but its appearance is not normal and the total length of the constricted portion exceeds two inches.

Sections from the ascending aorta stained by Mallory's connective tissue stain show an increase in the amount of fibrous tissue, particularly in the region of the vasa vasorum (a region especially affected in syphilitic diseases of the aorta), but the distribution in this case is too diffuse to be suggestive of syphilis. Sections from the stenosed regions show a similar change, but the amount of thickening is greater, and muscular and elastic elements make up the bulk of the increase. Sections of the femoral artery show a surprising degree of fibrosis in both medial and adventitial coats and much of the intima beneath the endothelium shews a fibrous change: muscular elements are sparse, but the evidence of hypertrophy of the muscle is shewn by the prominence of the delicate longitudinally-running muscle fibrils in the intima, probably an early hypertrophic stage of arteriosclerosis. Microscopically the left brachial artery shews considerable hypertrophy of the middle coat, due to increase of the muscular elements, but there is also a patchy fibrosis: here the arteriosclerosis is less well developed than in the femoral artery.

The right kidney was not abnormal in appearance, but microscopically the vessels all show some sclerosis and the glomeruli in some areas are fibrotic. The left kidney was considerably smaller than the right: its capsule was thickened and adherent, and microscopically the secreting elements was found to be disorganized by a diffuse fibrosis: the glomeruli show pericapsular thickenings, adhesions, and hyaline transformation, and many of the tubules are distorted almost beyond recognition into cystic spaces containing hyaline casts. Microscopic cysts are present and the vessels throughout show widespread fibrosis of their coats. The changes are

so advanced in this kidney that they suggest a congenital mal-development of the organ as the basis upon which subsequent changes of vascular, or possibly inflammatory, origin have been superimposed.

## Discussion.

The most interesting clinical feature of this remarkable case was the curious cyanosis of the left hand, which in association with cardiac hypertrophy and in the absence of signs of paresis or venous obstruction, first suggested the correct diagnosis. The extremely high pressure in the brachial arteries in contrast with the almost normal level in the femorals furnished indisputable evidence in favour of coarctation.

At the post-mortem it was thought that arteriosclerosis might be found only in the vessels exposed to high pressure, but from the microscopical examination it is clear that this was not the case, for the changes in the femoral artery were more advanced than those in the brachial and there was also considerable sclerosis of the renal and splenic arteries.

As is well known, Bonnet has described two main types of coarctation, the 'adult' and 'infantile.' In the former the stenosis is so limited in extent that the aorta appears to have been ligatured at a point close to the insertion of the ductus arteriosus, which is never patent. Bonnet believes that this type is due to abnormal extension of the tissue of the ductus arteriosus into the wall of the aorta with subsequent contraction as the ductus is obliterated. Clearly our case has no resemblance to this variety.

In the infantile type the stenosis is frequently limited to the so-called isthmus of the aorta (the part that lies between the subclavian artery and the ductus arteriosus which is not much used during intra-uterine life), and Bonnet considers it to be due to failure of development and draws attention to the fact that with it are frequently associated other congenital abnormalities, particularly in the structure of the heart.

In our case the stenosis spreads widely beyond the true isthmus and the only evidence of other congenital abnormality is to be found in the condition of the left kidney, and there not with certainty. Bonnet himself recognized that there were many anomalous cases for which his hypothesis did not account very satisfactorily, and ours appears to be one of them. It may be that the diffuse arteriosclerosis in some way accentuated an original maldevelopment of the isthmus.

Our thanks are due to Dr. Jerome of Sutton Coldfield, and Dr. Tandy, R.M.O. at the Children's Hospital, without whose aid the post-mortem examination could not have been carried out.

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# HEREDITARY HYPERTELORISM WITHOUT MENTAL DEFICIENCY

BY

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Some years ago Greig[1] described 'a hitherto undifferentiated congenital cranio-facial deformity.' To the condition he gave the name 'Ocular hypertelorism.' The salient peculiarity of the condition is the great breadth separating the inner canthi. The abnormality results from the mal-development, commencing in early embryonic life, of the portion of the sphenoid which is laid down in cartilage. The great wings are undersized, and the lesser wings are hypertrophied and pass outwards to produce the characteristic changes in the face and skull. Some consequent degree of mental deficiency would be expected to coexist. Mental defect is a frequent concomitant of imperfect sphenoidal development. Strabismus is commonly associated with the disorder.

In the case which I have the opportunity of describing, the cranio-facial distinctions are marked but mental deficiency is absent.

Marion B., (Fig. 1), aged two years and one month, was admitted to my wards at Booth Hall Infirmary for Children, Manchester, on the fourth of June of this year suffering from acute bronchitis, a condition to which she is especially disposed.

FIG. 1.

*Family History.* The parents were not blood relations. The mother was hyperteloric. Although active and sensible she was very emotional. She was thirty-nine years of age when the patient, her first child, was born. Unfortunately I was unable to see her for more than a few moments as she was literally hurrying to hospital to be confined. And, again it is regretted, the mother's death took place a few days later from a puerperal complication. There is no photograph of this parent extant, but, in the words of the father, 'When you look at Marion's face you look at her mother's also.'

The second child, a male, presents no anatomical peculiarities. There is no history of miscarriage. The father was forty-nine years old at the time of the birth of the patient. He is alert and of fair intelligence. There is some evidence of old rickets. Except for the emotionalism of the mother there is nothing indicative of nervous stigmata or instability.

The pregnancy was normal and the child was born without undue difficulty. The weight at birth was two kilogrammes.

FIG. 2.

The child is 81 cm. in height and weighs 11·8 kgrm. She is able to walk well but stands with the weight of her body on the left foot and the right leg slightly abducted (Fig. 3). There is some right genu valgum. The epiphyses are enlarged and the radiologist reports that the X-ray of the wrist shows early evidence of rickets. The bones of the skull are thin. The skin is sallow but smooth. There is no acrocyanosis. While the hands and feet are plump they show no disproportions. Subcutaneous tissue is fairly well marked (Fig. 3). A small umbilical hernia is present. The face appears symmetrical. It is interesting to mention that Lightwood and Sheldon[2] describe a case of right-sided (unilateral) hypertelorism, and Fridolin[3] published a case of plagiocephaly which Greig considers to be partly hyperteloric.

Although at times the facial expression is bright and happy it is generally one of apathy. The mouth is open, but this is probably related to the presence of hypertrophied tonsillar and adenoid tissue. The forehead is broad and the frontal eminences are unusually prominent. There is some flattening of the occipital region but the vertex is only slightly raised (Fig. 2). Her eyes are placed widely apart. There is no ptosis nor definite strabismus A longitudinal mesial depression, 30 mm. in length, passes to the tip of the broad nose. The nasal bridge is flattened and the tip is retroussé. On examining the mouth it is found that the teeth are good but the incisors have the appearance of molars, the palate is not unduly arched, and the tongue is active and not enlarged. The anterior fontanelle can be felt, but is closed. Sight, hearing

FIG. 3.

and articulation are good and the vocabulary is no more limited than would be anticipated in a child of two years. The second mitral sound is accentuated but no murmur can be detected.

Measurements of head: The maximum horizontal circumference of the skull, measured round the most prominent parts of the glabella and occiput, is 480 mm. The greatest length, estimated from the most prominent part of the glabella to the most prominent part of the occiput, is 150 mm. The greatest parietal breadth, taken behind and above the temporal line, is 120 mm. The skull is thus brachycephalic, the cephalic index being 80. The facial length, from pogonion to nasion is 70 mm. The maximum bizygomatic width is 115 mm. The total facial index is thus 61. The highest point of the vertex is 70 mm. above the external auditory meatus. The distance between the inner

canthi is 40 mm. The two sets of orbital measurements are identical. The supraorbital notch is 35 mm. from the sagittal line. The greatest width of the orbit is 40 mm. and the greatest height 30 mm.

Mental condition: The child is extremely emotional. The appearance of a stranger at once excites and frightens her. She weeps on any provocation. She prefers to sleep upon the floor, and by her father alone can she be prevailed upon to go to bed.

With the exception of these features no evidence of impaired mentality can be detected. There is no history of convulsions.

## Discussion.

The important features of this case are the indications of hereditary origin of the anatomical peculiarities and the absence of mental deficiency. The ages of the parents at the time of the patient's birth are noteworthy.

Ogilvie and Posel[4] cite a case of oxycephaly whose mother and mother's cousin, also a female, showed similar characteristics. The more remote relative is reported to be mentally deficient.

A hyperteloric child without mental defect is described by Abernethy[5]. The mother, the mother's brother, and possibly the maternal grandfather show evidence of ocular hypertelorsim.

Mental deficiency and hypertelorism were present in a case quoted by Reuben and Fox[6]. Two cousins had hyperteloric features and the writers emphasize a familial tendency to myopia.

I wish to thank Dr. J. D'Ewart, the medical superintendent, for his permission to publish the case, Mr. Spaven for his report on the teeth, and Dr. Reed for his radiological examination.

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# NOTE ON A FAMILY WITH BRACHYDACTYLY

BY

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The accompanying photographs show brachydactyly of both hands and feet in a child, its mother and aunt ; the great-grandmother, grandmother and uncle are said to have presented similar deformity. The shortening of the of the digits is of the type associated with apparent absence of the middle phalanges. The mother is unable to state whether any other members of the family have been affected.

Brachydactyly is a deformity of more than usual interest for two reasons : first, because Bateson[1] states that it is the first human condition found to obey Mendelian laws, being a dominant characteristic ; and secondly, because there appears to be a considerable number of different forms of brachydactyly.

Feil[2] states that diminution in the length of the fingers is much more rare than other malformations such as polydactyly and ectrodactyly ; that the hands are more commonly affected than the feet ; and that one or both hands and one or several digits may be involved. He classifies the condition into :—

(1) Brachydactyly by simple shortening of the digits, the number of bones remaining normal.
(2) Brachydactyly by ankylosis of the bones of the digit.
(3) Brachydactyly by partial loss of bone, either in metacarpus or phalanges.

Drinkwater[3] describes a Liverpool family in which there occurred in several generations a brachydactyly exactly like that illustrated herewith. He considered that the second phalanx is not really absent, but at a certain stage of development has united with the terminal phalanx to form a bone of which ' the pyramidal distal portion corresponds to the ungual phalanx and the basal cubical portion ot the middle phalanx.' In the case here reported (Figure 9), there appear to be rudimentary middle phalanges which have not fused with the terminal ones. I have been unable to trace any kinship between the Liverpool family and the Belfast family which I describe.

Gilmore[4] describes a family where one child had two phalanges for each finger, but had normal feet, and whose brother had other deformities such as webbed toes or absence of nails.

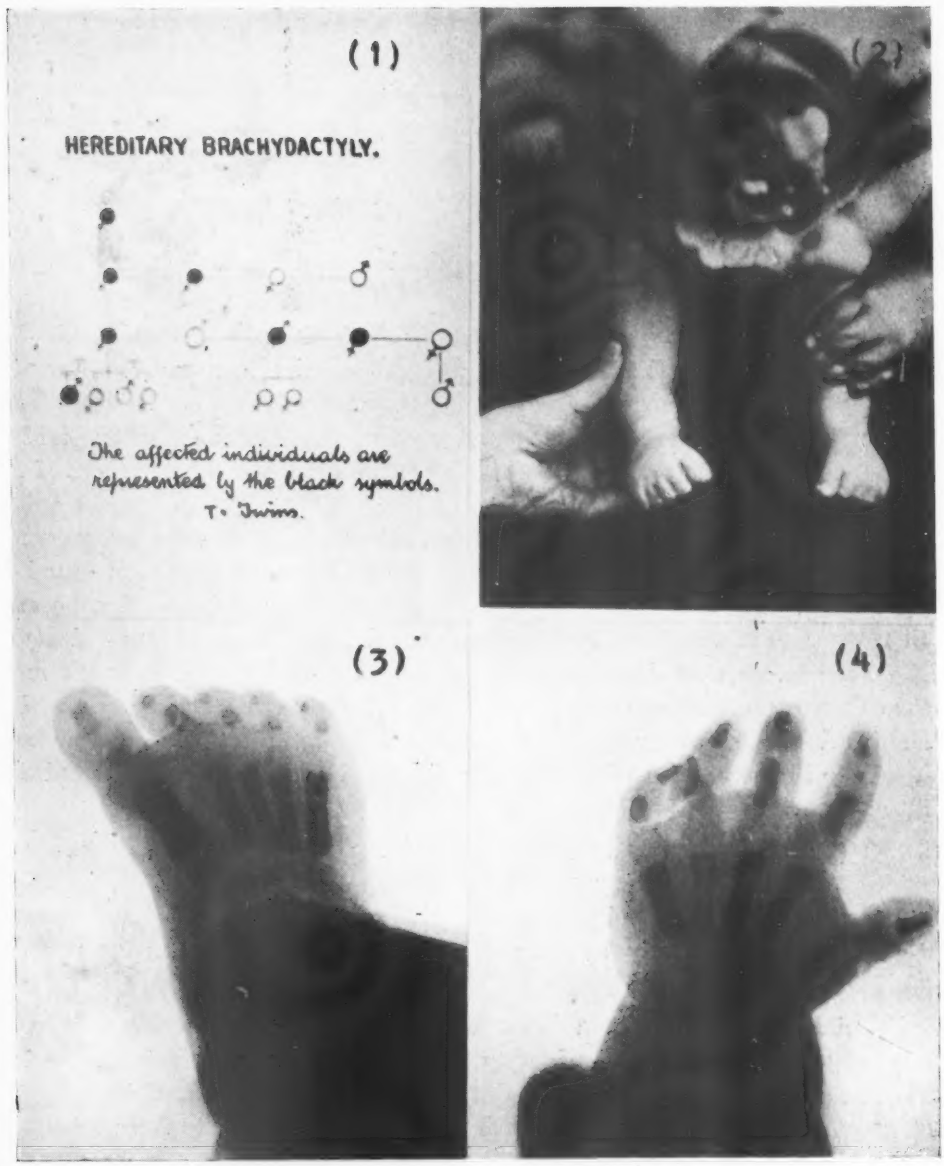
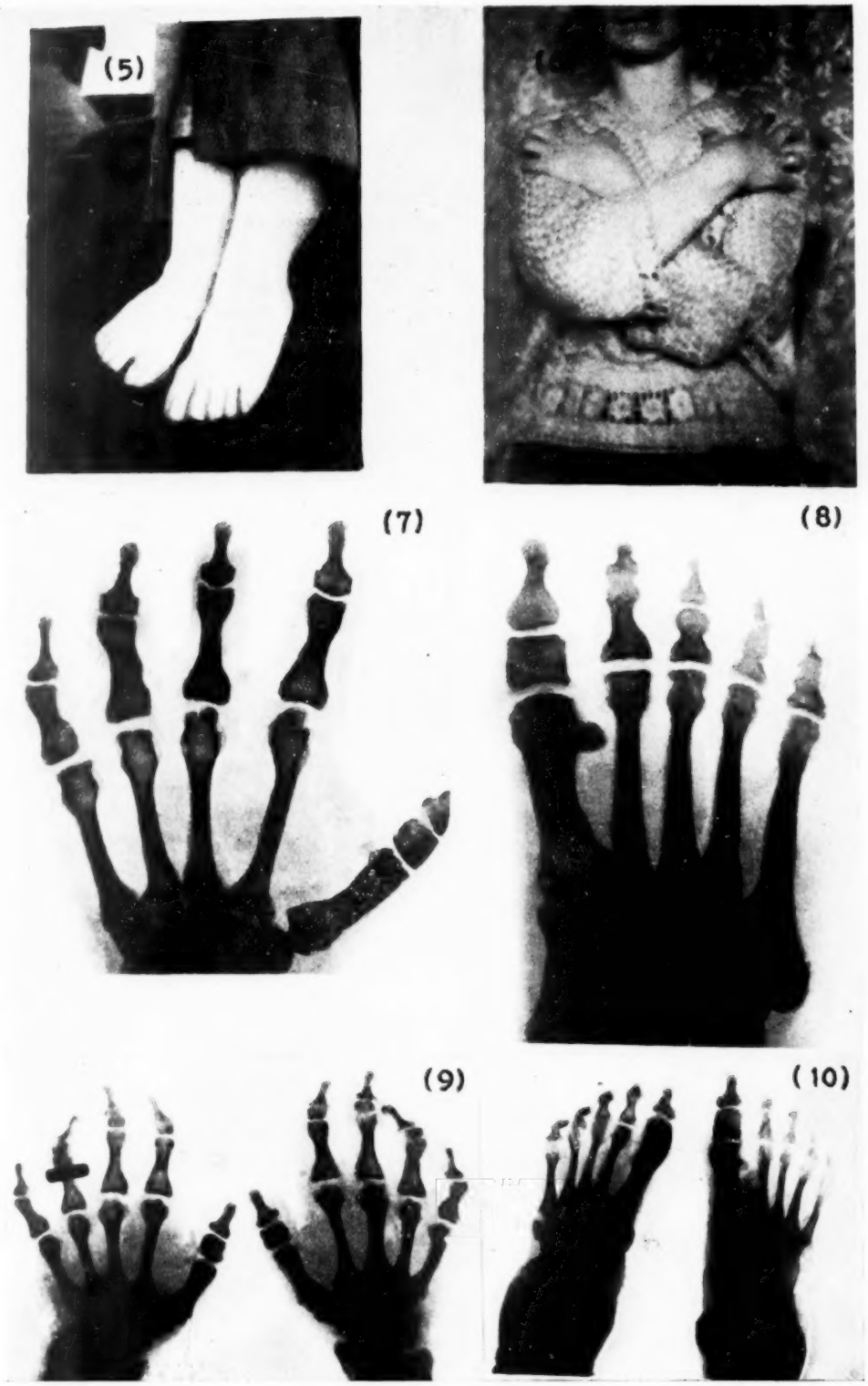



Fig. 1. Table showing incidence of brachydactyly.
Fig. 2. Photograph of the child, held by the mother.
Figs. 3 & 4. Radiograms of the child's foot and hand.




Figs. 5 & 6. The mother's feet and hands.
Figs. 7 & 8. Radiograms of the mother's hand and foot.
Figs. 9 & 10. Radiograms of the aunt's feet and hands.

Walker[5] reported a family in which there occurred imperfect union of first and second phalanges in the ring and middle fingers. Feil[2] says that the phalangeal types of brachydactyly are less rare than those in which there is shortening of one or more of the metacarpal bones (usually that of the ring finger). Such cases have been reported by Boorstein[6] and Wagner[7] amongst others.

References to this curious deformity appear to be rare in English medical literature.

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# METABOLIC STUDY OF AN ALKAPTONURIC INFANT

BY

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and

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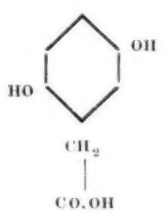
Alkaptonuria is an extremely rare condition, which is due to a defect in protein metabolism. The most probable explanation is that it is due to the absence of the particular enzyme which normally effects a particular stage in the complete destruction of tyrosine and phenyl-alanine. Alkapton is the intermediate product beyond which metabolism can no further go, and it is excreted as such in the urine. The defect is congenital and it is inherited, although the line of inheritance is difficult to trace. Transmission is seldom direct from parent to child, but several children in one family may be affected. Consanguinity between parents seems to have some responsibility for its occurrence. It is probably a Mendelian recessive characteristic. It is more common in males than in females. It may give rise to pigmentation of the cartilages and to arthritis.

Very little has been written on the subject since the publication of Sir Archibald Garrod's[1] book on 'Inborn Errors of Metabolism' in 1923. There he recounts the development of the knowledge of this metabolic disorder since the discovery in 1858 by Bödeker of a second reducing substance in the urine of a diabetic. He called it alkapton. In 1891, Wolkow and Baumann showed that the reducing substance was homogentisic acid, with the empirical formula $C_8H_8O_4$. This has been confirmed by several other workers, and its constitution definitely proved to be that of hydroquinone-acetic acid, with the following formula :—




Homogentisic acid is derived from those proteins which are rich in tyrosin and phenyl-alanine. The administration by mouth of tyrosin or phenyl-alanine, or of proteins rich in these substances, to an alkaptonuric, leads to an increased output of alkapton in the urine. During starvation the amount

of alkapton in the urine diminishes but does not disappear entirely. Some is derived, it is therefore deduced, from body protein also. On a more or less average mixed diet, the amount of alkapton in the urine bears a constant relationship to the total amount of nitrogen excreted in the urine. From the investigations made by different workers on different alkaptonurics, this ratio has been found to be roughly as 40: 100. But Gross and Allard, whose patient's diet contained a large quantity of milk, found the ratio to be 60–70 : 100. Most of the cases investigated have been adults, but in 1911 Katsch[3] published a full report on the nitrogen metabolism in an alkaptonuric child 3 years of age. His findings correspond to those of other workers, but with this exception : during a starvation period of three days, the homogentisic acid output fell, until on the third day it disappeared completely from the urine. There was, during this period, a corresponding rise in the output of acetone. A similar result was obtained during a period in which a diet of carbohydrate and fat with little protein, was given. Katsch assumes that in his case the homogentisic acid is further oxidized to acetone. That this may be so, there is some confirmation from Embden's experiment, in which he shows that if homogentisic acid is perfused through a normal liver it is converted to aceto-acetic acid.

Two questions seem to require answers :—

(1) Is homogentisic acid an intermediate product of normal metabolism, or is an alternative path in the metabolism of the aromatic-protein complex followed in an alkaptonuric ?

(2) Does the degree of inability to metabolize the aromatic-protein complex vary ; or, in other words, is the error maximal ?

That it is an intermediate product of normal metabolism is supported by the fact that normal individuals can ingest homogentisic acid without producing alkaptonuria. It is also supported by Katsch's findings : but these, obviously, confute the suggestion that the error is maximal.

Dakin[5] especially holds to the view that the formation of homogentisic acid is abnormal, and that a path other than normal has been followed in the metabolic process. He seems to have proved, at least, that alternative paths exist.

Garrod supports the intermediate product theory, and holds to the view that the error is maximal, basing his opinion on the constancy of the ratio of homogentisic acid to nitrogen ; but he says : ' If in alkaptonuria the error were complete and maximal, all subjects of that anomaly, when fed upon a given standard diet, should excrete equal quantities of homogentisic acid, and changes in quantities consumed should leave the ratio of homogentisic acid to nitrogen undisturbed. . . . It would be necessary to place a number of alkaptonurics upon a standard diet, in which not only are the proteins the same, but in which also the several proteins are in uniform proportions. These conditions would be best fulfilled by milk alone.' Further he says : ' If it can be shown that, on absolutely the same diet, the homogentisic acid to nitrogen ratio is far above the average in some cases . . . it will be proved that the uniformity of the homogentisic acid to nitrogen ratio does not indicate complete conversion of tyrosin and phenyl-alanine into homogentisic acid.

We shall be driven to conclude that the katabolism of some part of these aromatic fractions of proteins of the food and tissues habitually follows some other path than that through homogentisic acid.'

### Case Report.

Gordon M., born on 29th August 1928, and first seen in January 1929, is the first child of healthy parents, who are not consanguineous, and who do not know of the existence of the anomaly under discussion in any of their antecedents. His mother stated that the child's urine had been very dark at intervals of several days since birth. She also stated, with conviction, that the child had attacks of abdominal pain at those times when the urine passed was not so dark. She brought with her a napkin stained a deep chocolate colour, and she had the wisdom to bring the child unwashed. He looked perfectly healthy and well-developed, presenting no abnormality except a deep brown staining of the thighs and lower abdomen. A specimen of urine obtained gave a positive reaction to tests for alkapton.

He has been in hospital on two occasions during which were made the investigations whose results are set out below: from 26th February until 23rd March, when his weight varied from 12 lb. 10 oz. to 12 lb. 14 oz.; and from 22nd May to 26th June, when his weight varied from 13 lb. 12 oz. to 13 lb. 8 oz. He attended the out-patient department in the interval. He was in very good health until the first week in May, when he became peevish, looked pale and unwell, and his mother complained that he had attacks of pain. This state continued for about four weeks, and no cause was found except that he was cutting teeth. Some of his pain may have been associated with micturition.

The urine varied in colour, sometimes dark when passed, sometimes dark on standing, but at no time, except during starvation, was alkapton absent. By 'dark' is meant a pinkish, smoky brown colour, which gave place rarely to a deep chocolate colour. On many occasions the appearance of the urine did not suggest any abnormality to the uninitiated, and it is quite easy to understand why a life-long history of the abnormality is not always obtained. His Wassermann reaction was negative.

### Metabolic Investigations.

The investigations were made during seven periods, and to explain each period in turn seems to be the simplest plan.

Period 1. March 7—13. Diet=Milk, 24 oz.—For seven consecutive days he was fed on milk only. The urine was collected continuously and removed every 3 hours, and the total nitrogen and total alkapton excretion in 24 hours estimated. The presence or absence of acetone was noted daily (Table 1).

TABLE 1. March 7—13.

| In grammes | 7th | 8th | 9th | 10th | 11th | 12th | 13th | Average |
|---|---|---|---|---|---|---|---|---|
| Total N. in 24 hr. | 1·33 | 1·53 | 1·67 | 1·89 | 1·30 | 1·17 | 1·43 | |
| Total Homogent. Ac. in 24 hr. ... | ·79 | ·75 | 1·01 | 1·07 | ·83 | ·75 | ·76 | ·85 |
| Ratio $\frac{\text{H.A.}}{\text{N.}}$ ... | $\frac{59}{100}$ | $\frac{49}{100}$ | $\frac{73}{100}$ | $\frac{56}{100}$ | $\frac{64}{100}$ | $\frac{64}{100}$ | $\frac{53}{100}$ | $\frac{60}{100}$ |
| Acetone ... ... | — | — | — | + | trace | — | — | |

Period 2. March 14—20. Diet=Milk, 30 oz. and egg yolk, 2 dr.—On March 14th, egg yolk was added to the milk, and the amount of milk was increased. Egg yolk is rich in tryosine, and we would expect that the output of alkapton would be increased. Estimations as before were made, after the child had been on this diet for three days (Table 2).

TABLE 2. March 18—20.

| In grammes | 18th | 19th | 20th | Average |
|---|---|---|---|---|
| Total N. in 24 hours ... ... | 1·40 | 1·83 | 2·46 | |
| Total Homogent. Ac. in 24 hr. ... | ·73 | 1·01 | 1·69 | 1·14 grms. |
| Ratio $\frac{\text{H.A.}}{\text{N.}}$ ... ... ... ... | $\frac{52}{100}$ | $\frac{55}{100}$ | $\frac{69}{100}$ | $\frac{59}{100}$ |
| Acetone ... ... ... ... | trace | — | — | |

The child was at home from 21st March to 22nd May, when his diet consisted of milk and carbohydrate. Potassium iodide, which is said to diminish the output of alkapton in the urine, was prescribed, but as his mother omitted to give it during the week before his re-admission to hospital, we repeated this experiment at a later date.

Period 3. May 22—31. Diet = Milk 30 oz.—After re-admission, the child was given milk only, and examinations made as before on the last three days of this period (Table 3).

TABLE 3. May 29—31.

| In grammes | 29th | 30th* | 31st | Average (29th & 31st) |
|---|---|---|---|---|
| Total N. in 24 hours ... ... | 1·27 | 1·08+ | 1·93 | |
| Total Homogent. Ac. in 24 hr. ... | ·5 | ·35+ | ·60 | ·55 |
| Ratio $\frac{\text{H.A.}}{\text{N.}}$ ... ... ... ... | $\frac{38·9}{100}$ | $\frac{32·8}{100}$ | $\frac{30}{100}$ | $\frac{34}{100}$ |
| Acetone ... ... ... ... | — | — | — | |

*Some urine lost.

Period 4. June 1—6. Diet = Milk, 30 oz. and yolk of 1 egg.—Egg yolk was now added to the diet, but no alteration was made in the quantity of the milk. After three days, specimens were again collected and similar estimations made (Table 4).

TABLE 4. June 4—6.

| In grammes | 4th | 5th | 6th | Average |
|---|---|---|---|---|
| Total N. in 24 hr. ... ... | 2·5 | 2·58 | 2·6 | |
| Total Homogent. Ac. in 24 hr. ... | ·71 | 1·16 | 1·15 | 1·01 |
| Ratio $\frac{\text{H.A.}}{\text{N.}}$ ... ... ... ... | $\frac{28·2}{100}$ | $\frac{45·1}{100}$ | $\frac{48·1}{100}$ | $\frac{40·5}{100}$ |
| Acetone ... ... ... ... | trace | trace | — | |

As already stated, before the time of his re-admission up to this point, the child was not so well as previously, and he lost weight. He was peevish and looked pale and out of sorts. There was no fever, and no explanation found besides the fact that he had cut his third, and had almost cut his fourth tooth. From May 31 to June 6, the stools were large, although there was not a frank diarrhœa,

Period 5. Diet=Water.—In order to see whether in our case, as in Katsch's case, alkapton would be replaced by acetone during starvation, water only with a small quantity of sugar was given for 36 hours. Urine was collected continuously and removed every three hours. The presence or absence of alkapton in each specimen was determined by the addition of a few drops of ammonia to 1 c.cm. of urine. If alkapton is present a brown colour is at once obtained, and the depth of the colour is an indication of the amount of alkapton present. We noted a gradual diminution in colour until in the 11th specimen it was entirely absent. No urine was passed in the last three hours. At the end of 36 hours starvation, milk was again given, and within three hours the deep colour of the urine returned when ammonia was added. Other estimations were made as before (Table 5).

TABLE 5. JUNE 6–8.

| In grammes | 6th—7th | 7th | 7th—8th |
|---|---|---|---|
| Total N. in 24 hrs. ... ... | Water 24 hr. 1·31 | Water 12 hr. ·23 | Milk 12 hr. ·59 |
| Total Homogent. Ac. in 24 hr.... | ·02 | ·007 | ·29 |
| Ratio $\frac{\text{H.A.}}{\text{N.}}$ ... ... ... ... | $\frac{1·7}{100}$ | $\frac{3·1}{100}$ | $\frac{49·4}{100}$ |
| Acetone ... ... ... ... | + | trace | |

Katsch found that homogentisic acid was absent from the urine in the third day of starvation in his child 3 years of age. In our case, homogentisic acid disappeared by the middle of the second day. We did not find, however, that the output of acetone in the urine or in the breath was any greater at this time than at any other time. Had we not examined the urine at frequent intervals, the fact that homogentisic acid was absent after 30 hours' starvation would have been missed. A striking feature at this point is the prompt return of homogentisic acid to the urine on the administration of a homogentisic-acid-producing food.

Period 6. June 8—14. Diet=Milk 32 oz.—The child was now in much better health, and was again given a diet of milk. After three days, the total urine output was collected on three successive days, and the same estimations repeated (Table 6).

TABLE 6. JUNE 12—14.

| In grammes | 12th | 13th | 14th | Average |
|---|---|---|---|---|
| Total N. in 24 hr. ... ... | 2·66 | 2·60 | 3·13 | |
| Total Homogent. Ac. in 24 hr. ... | 1·53 | 1·38 | 1·73 | 1·55 |
| Ratio $\frac{\text{H.A.}}{\text{N}}$ ... ... ... ... | $\frac{58}{100}$ | $\frac{54}{100}$ | $\frac{55}{100}$ | $\frac{56}{100}$ |
| Acetone ... ... ... ... | trace | — | — | |

Period 7. June 15—25. Diet=Milk, 32 oz. Potassium iodide 1½ gr.—To decide the possible responsibility of potassium iodide for the low figures obtained during Periods 3 and 4 the child was now given 1½ gr. daily for a week, and on the same diet, estimations were again made for comparison with those in Table 6.

TABLE 7. JUNE 24 AND 25.

| In grammes | 24th | 25th | Average |
|---|---|---|---|
| Total N. in 24 hr. ... ... ... | 2·32 | 2·79 | |
| Total Homogent. Ac. in 24 hr. ... | 1 27 | 1·82 | 1·54 |
| Ratio $\frac{\text{H.A.}}{\text{N.}}$ ... ... ... ... | $\frac{55}{100}$ | $\frac{65}{100}$ | $\frac{60}{100}$ |

## CONCLUSIONS.

When the child was in good health and having a diet of milk only, the daily output of homogentisic acid increased according to the total intake of milk: ·75 to 1·07 grm. when having 24 oz., and 1·53 to 1·82 grm. when having 32 oz. The ratio to nitrogen remained practically constant, averaging in the first case 60 to 100, and in the second case 56 to 100.

While the child was unwell and on a milk diet, the output of homogentisic acid fell to ·55 grm. daily, and its ratio to nitrogen fell to 34 to 100. That this was not due to the administration of potassium iodide may be accepted, for a similar fall was not repeated after a week's continuous administration of potassium iodide. The ratio then remained at 60 to 100. It is more probably an indication of the general metabolic upset due to teething, for it is associated with a loss in weight and with a fall in nitrogen retention, although the three things are not quite simultaneous.

In our first experiment with egg yolk, very little was given, and the result was further confused by the fact that the amount of milk was increased. In our second experiment, these mistakes were avoided, and the results obtained show a definite increase in the total daily output of homogentisic acid, and a rise in its ratio to total nitrogen. This is in agreement with the findings of previous workers.

During starvation, homogentisic acid disappeared from the urine after 30 hours. Katsch found that it disappeared in the case of a child of 3 years on the third day. In adults, alkapton is said to persist in the urine during starvation. May this not indicate the degree of retention in older patients rather than the production of alkapton from the body proteins? During starvation, also, we did not note a degree of acetonuria greater than at any other time.

## FURTHER EXAMINATION OF THE URINE.

The nitrogen partition in the urine of normal infants is a subject on which opinions vary, but that the urea nitrogen is high seems to be a common finding. Abt[6] quotes Camerer, Talbot, and Meyer and Rietschel, whose figures range from 60—83 per cent. of total nitrogen.

In alkaptonuria, Gibson and Howard[4] found low urea nitrogen, high ammonia nitrogen, high uric acid nitrogen, and high undetermined nitrogen. They quote Rayold and Warren as finding the urea below the average and

the uric acid diminished. Lusk, in his 'Science of Nutrition,' writes 'the distribution of the several nitrogenous constituents in alkaptonuria is said to remain normal.'

The figures which we give have been obtained from examination of the total urine on each of six days, while the child was having milk only. Accepting Abt's figures as normal, in our alkaptonuric the urea nitrogen is certainly low and the ammonia nitrogen is not high. The uric acid nitrogen is high, but the presence of homogentisic acid may have rendered this estimation inaccurate. The undetermined nitrogen is high.

TABLE 8. DIET = MILK.

| | Volume c.cm. | Total N. in grm. | Urea N. | Ammon. N. | Uric acid N. |
|---|---|---|---|---|---|
| 29th May ... ... | 285 | 1·268 | ·356 | ·106 | ·151 |
| 30th ,, ... ... | 225+ | 1·075+ | ·279+ | ·057+ | ·110+ |
| 31st ,, ... ... | 427 | 1·931 | ·425 | ·137 | ·167 |
| Average % of total N. | | | 24·8% | 7% | 10% |
| 12th June ... ... | 641 | 2·658 | 1·069 | ·191 | ·317 |
| 13th ,, ... ... | 780 | 2·593 | ·568 | ·417 | ·460 |
| 14th ,, ... ... | 750 | 3·131 | ·738 | ·754 | ·540 |
| Average % of total N. | | | 28·6% | 15·8% | 15·7% |

The relative rate of excretion of nitrogen and homogentisic acid is also disputed. Some workers have found that a fall in nitrogen excretion accompanies a rise in homogentisic acid excretion; while others have found that a rise in the one is accompanied by a rise in the other. Katsch found that during three days of protein-free diet, the nitrogen excretion rose while the homogentisic acid excretion fell, and when the protein was added to the diet, the nitrogen excretion fell while the homogentisic acid output rose. Reference to our tables shows that a rise in homogentisic acid is always accompanied by a rise in nitrogen in the urine, while a fall in homogentisic acid is accompanied by a fall in nitrogen. The greatest variation is shown in the starvation period: both fall, but the homogentisic acid falls much more than the nitrogen. This may be explained by the finding of Abderhalden and Block (quoted by Lusk[2]) that the addition of water to an otherwise constant diet caused an increase in the nitrogen of the urine, due to a washing-out of nitrogen end-products. There is, presumably, in this case, little or no retention of homogentisic acid in the tissues, for it disappeared from the urine after 30 hours' starvation. The return of homogentisic acid to the urine within 3 hours of the administration of milk, shows the rate of metabolism of the aromatic fraction of the protein and rate of excretion. The prompt return of the HA. to N. ratio to that found immediately before 36 hours' starvation, suggests that metabolism of all protein fractions occurs simultaneously (Table 9).

TABLE 9.

| In grammes | Milk 24 hr. 5—6 June | Water 24 hr. 6—7 June | Water 12 hr. 7 June | Milk 12 hr. 7—8 June |
|---|---|---|---|---|
| Nitrogen ... | 2·6 | 1·31 | ·23 | ·59 |
| HA. ... ... | 1·15 | ·02 | ·007 | ·29 |
| HA. to N. ... | 48·1 : 100 | 1·7 : 100 | 3·5 : 100 | 49·4 : 100 |

The acidity of the three hourly specimens of urine, 100 in all, was determined electrometrically, and it was found that the average pH range was from 5·43 to 6·7. On one occasion it was 7·16 and on one occasion 9·15. Lusk gives the normal range as 5·1—7·2. In alkaptonuria, then, the acidity is slightly greater than normal.

The depth of colour of the urine did not bear any constant relationship to its acidity, although the darkest specimen was that which had a pH of 9·15. The high acidity may be the reason for the dysuria, which certainly occurs from time to time.

### Protein metabolism.

Complete protein metabolism was studied during four periods of three days each—Period 1 (last 3 days), period 2, period 3, and period 4.

During periods 1 and 2, when the child was in good health, the average nitrogen intake was 4·02 grm., the average nitrogen absorbed was 93·75 per cent., and the average nitrogen retention 53·95 per cent.

During periods 3 and 4, during which time the child was unwell because of teething, the nitrogen retention fell to a low figure on the third day of Period 3, and remained low during the whole of period 4. The average nitrogen intake was 3·49 grm., the average nitrogen absorbed was 91·1 per cent., and the average nitrogen retention was 30·42 per cent. It is necessary to draw this distinction, in order to emphasize the point which we made concerning the low output of homogentisic acid during the two latter periods. The low total nitrogen retention, low homogentisic acid output, and loss in weight seem to be inter-related, although they are not entirely simultaneous (Tables 10 and 11).

During health, the nitrogen absorption and retention appear to be within normal limits, if compared with the results obtained in a hitherto unpublished study by one of us (E. M. H.) of the protein metabolism of a group of 23 babies fed on cow's milk. In them the average percentage absorption of nitrogen was found to be 88, with a range of 96—74, and the average percentage retention 49·7, with a range of 66—28.

TABLE 10.

| | | Nitrogen in grm. Av. total intake | Average total absorption | Average total retention | Average % absorption | Average % retention |
|---|---|---|---|---|---|---|
| In health | Period 1. 11—13 March ... | 2·76 | 3·53 | 2·2 | 93·9% | 58·6% |
| | Period 2. 18—20 March ... | 4·27 | 4·03 | 2·105 | 93·6% | 49·3% |
| Teething | Period 3. 29—31 May ... | 3·54 | 3·05 | 1·54 | 91·4% | 44·3% |
| | Period 4. 4—6 June ... | 3·45 | 3·13 | ·57 | 90·8% | 16·55% |

TABLE 11.

| Diet | Milk | | Milk+egg yolk | | |
|---|---|---|---|---|---|
| | 30th May | 31st May | 4th June | 5th June | 6th June |
| HA. to N.... | 32·8 : 100 | 30 : 100 | 28·2 : 100 | 45·1 : 100 | 48·1 : 100 |
| % N. retention | 50·8 | 25·85 | 23·1 | 9·3 | 17·26 |
| Weight ... | | 13 lb. 8 oz. | | | 13 lb. 6 oz. |


## Summary.

1. A case of alkaptonuria in an infant has been studied.
2. In health, on purely milk diet varied quantitatively, the homogentisic acid to nitrogen ratio is 55—60 : 100. This is very similar to the ratio found by Gross and Allard, whose patient, an adult, had a largely milk diet. It supports the ' maximal error ' theory.
3. When the nitrogen retention fell, the homogentisic acid to nitrogen ratio fell to 34 : 100.
4. After 30 hours' starvation, homogentisic acid disappeared from the urine. Acetone did not take its place.
5. The output of homogentisic acid was not diminished by the administration of potassium iodide.
6. There is no evidence to show that homogentisic acid is other than an intermediate product of normal metabolism.
7. The nitrogen partition in the urine differs from the normal. Most notable is the low urea nitrogen.
8. The acidity of the urine is slightly higher than normal.
9. Total nitrogen absorption and retention is normal.

We are indebted to Professor Leonard Parsons for his helpful criticism of this paper. The expenses of part of the work have been met by a grant from the Medical Research Council, to whom also we express our thanks.

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